Clinical Aspects of Critical Biologic Agents

May 2001

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Michigan Department of Community Health

Bureau of Epidemiology

Sponsored by the Public Health Consortium

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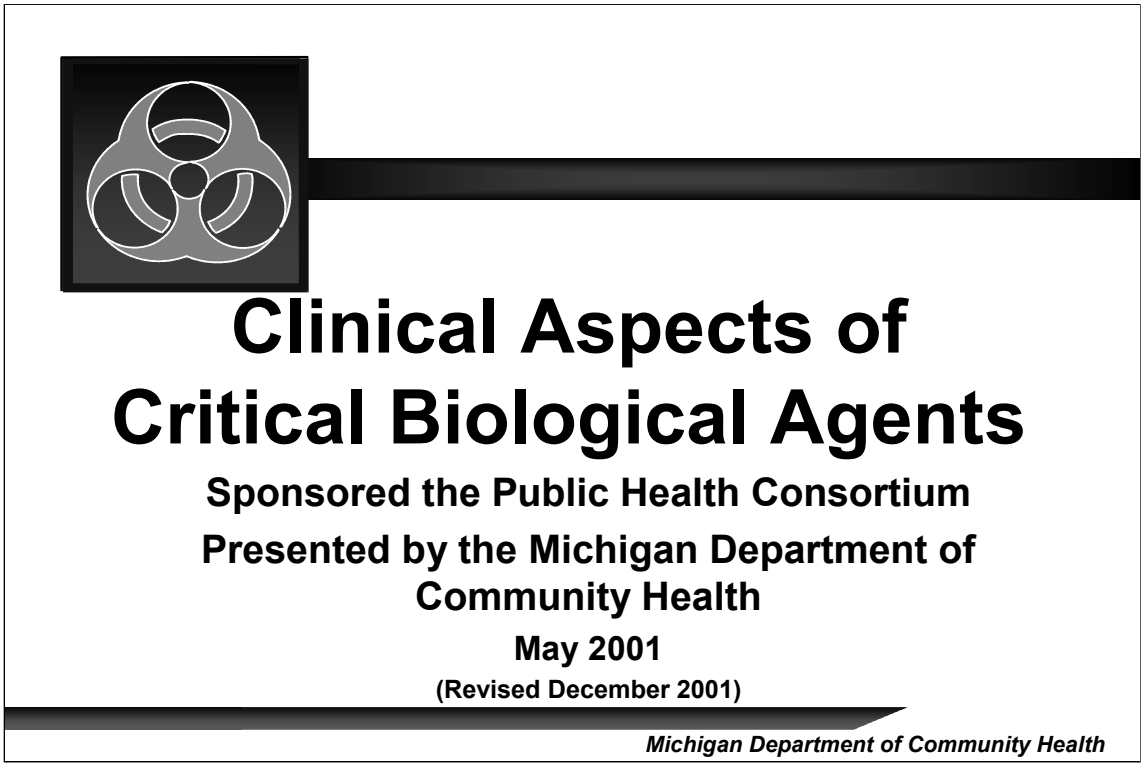
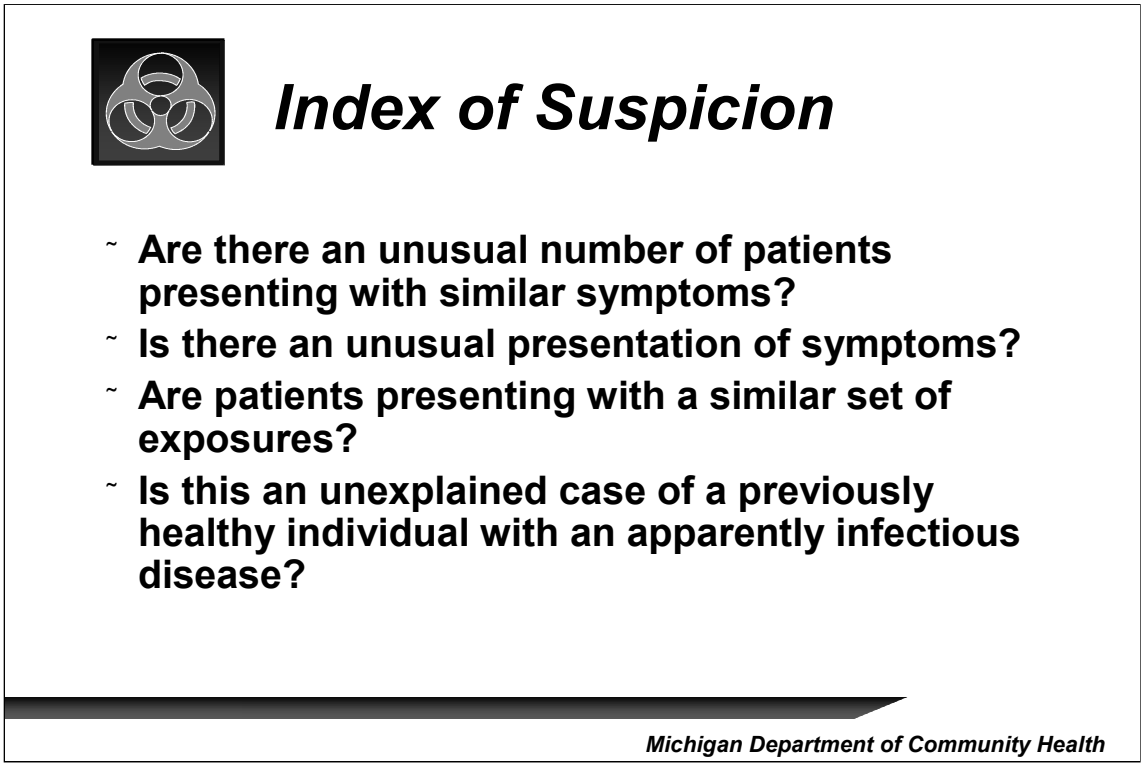


The Michigan Department of Community Health Surveillance Systems Section has compiled a series of slides that are designed to better prepare clinicians to identify and address exposure to critical biological agents. While not inclusive of all information, these slides provide a foundation of knowledge of dealing with these special circumstances of exposure.



Perhaps the most critical factor in identifying these agents lies in the clinicians ability to raise key questions. A clinician needs to always maintain an Index of Suspicion, even if screening or confirmatory laboratory work has not been completed. What are the Zebra's?

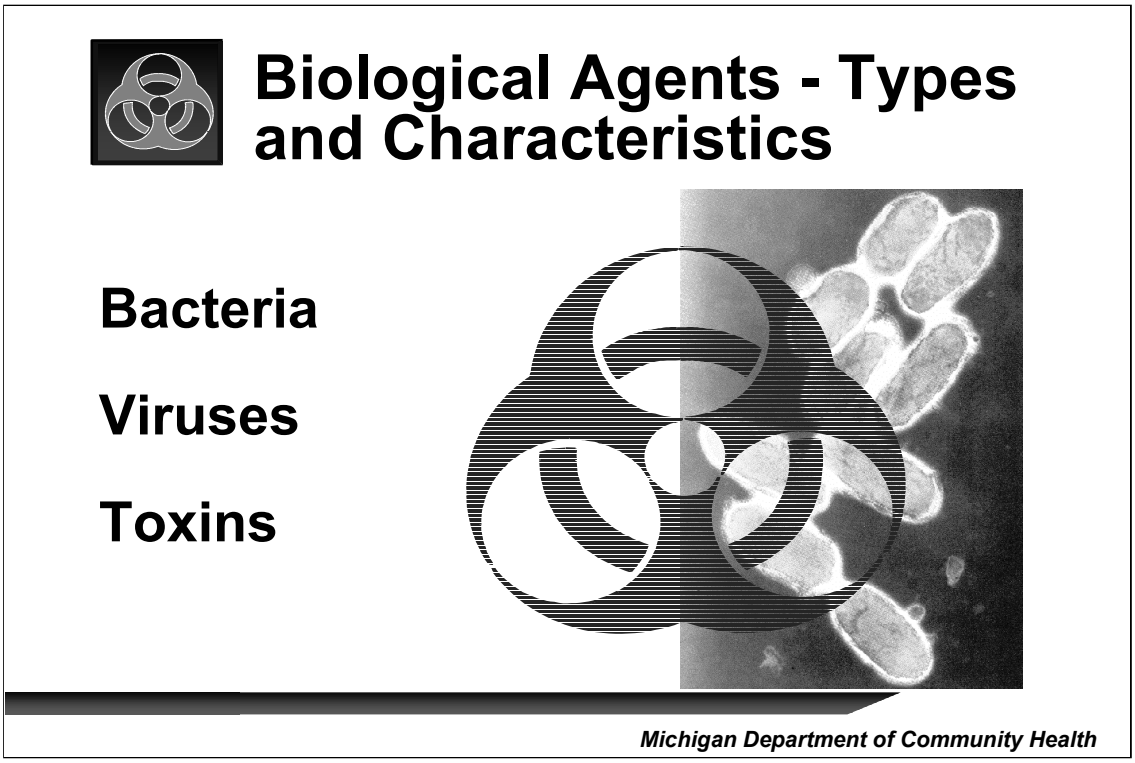
Are there an unusual number of patients presenting with similar symptoms?

Is there an unusual presentation of symptoms?

Are patients presenting with a similar set of exposures?

Is this an unexplained case of a previously healthy individual with an apparently infectious disease?

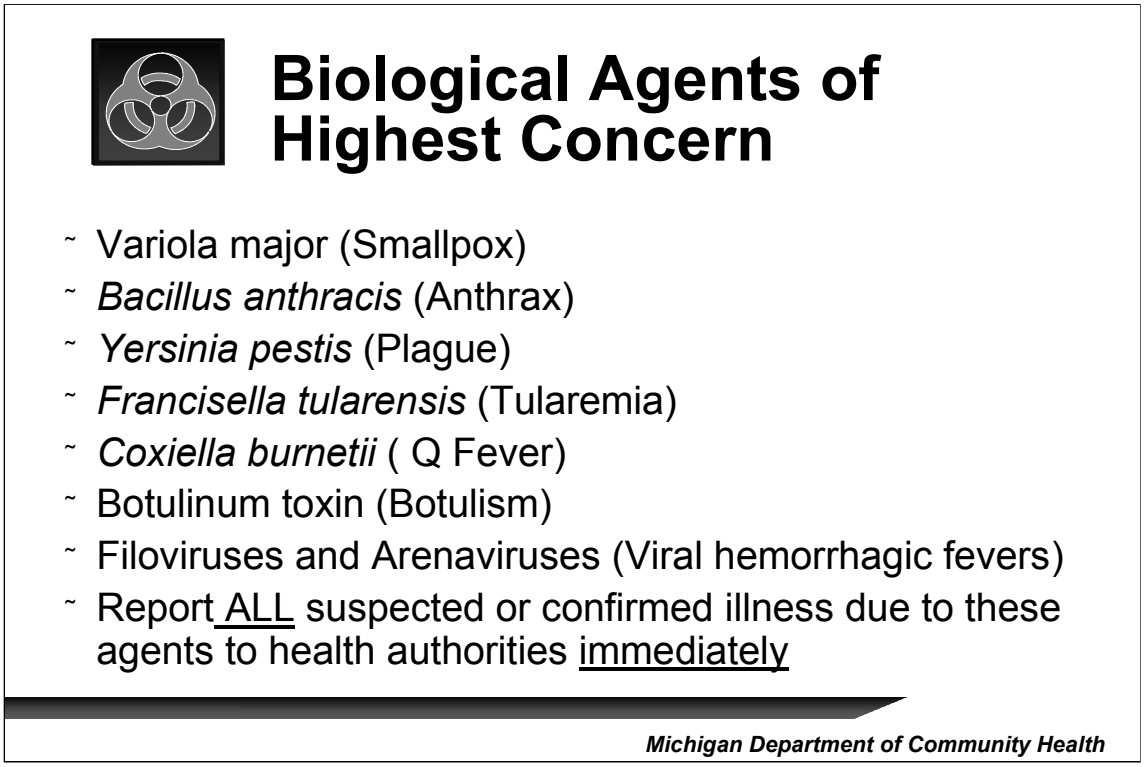
By asking these questions healthcare providers can facilitate rapid identification of these agents. Providers form the front lines in the control and treatment of communicable disease.



BIOLOGICAL AGENTS

Critical biologic agents fall into three types; Bacteria, viruses, and toxins. Each of these groups possesses it's own unique characteristics and challenges in diagnosis, treatment and prevention of secondary transmission.

NOTE: The organism pictured in the biohazard symbol above is Yersinia Pestis, the bacteria that causes all forms of plague.



The CDC has developed a list of agents of highest biological concern. The agents of highest priority for public health preparedness efforts are:

Variola major (smallpox)

Bacillus anthracis (anthrax)

Yersinia pestis (plague)

Fransicella tularensis (tularemia)

Coxiella burnetii (Q Fever)

Botulinum toxin (botulism)

and Viral Hemorrhagic Fevers due to Filo and Arenaviruses

All suspected or confirmed illness due to these organisms should be reported to health authorities immediately

The CDC considered many factors when determining which agents to put on the critical agent list. Priority was given to agents meeting the following criteria:

•Infectious by the aerosol route

•Stable enough to cause disease after aerosol release in the environment

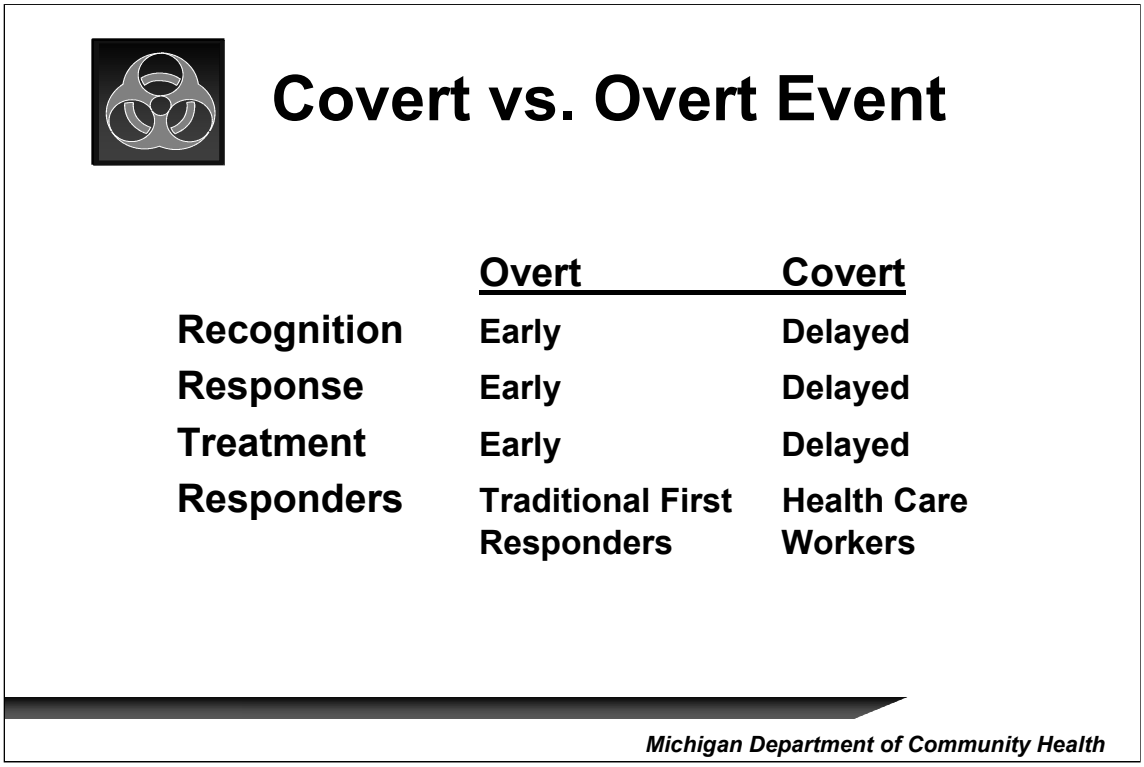
•A very high percentage of the civilian population is susceptible to infections caused by these agents

•Cause high morbidity and mortality

•Some are contagious person-to-person

•Many are difficult to diagnose or treat

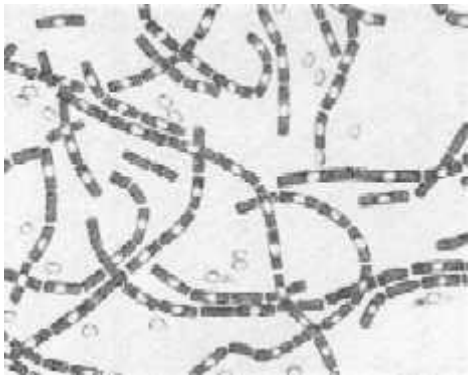
•Some have been previously developed as biological weapons



There are two different types of scenarios for a Bioterrorism event: an announced, or overt, attack; and an unannounced, or covert, attack. In an overt attack, recognition, response, and treatment will take place early on in the scenario and will primarily involve the traditional first responders (EMT's, Fire, Police, etc.). In a covert attack, recognition, response, and treatment will be delayed by as much as several days and will involve response from health care workers.

Anthrax: Overview

- Primarily disease of herbivores
- Humans usually infected by contact with infected animals or contaminated animal products
- Soil reservoir
- Woolsorter's disease (inhalation anthrax)
- No person-to-person transmission of inhalational anthrax



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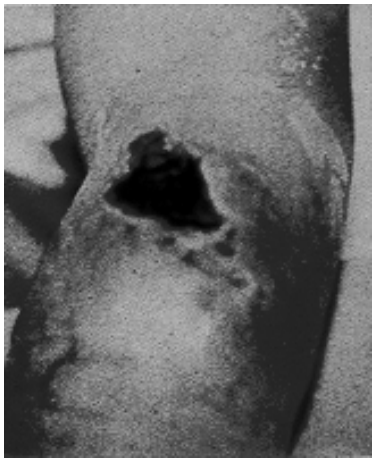
While *B. Anthracis* is an organism that is found in soil throughout the world, Anthrax is not a common disease – Only 4 reported human cases were identified in the U.S. between 1983 and 2000. When humans are infected it is normally via contact with contaminated animals or animal products. The inhalational form of anthrax (very rare) is usually found in persons exposed to aerosolized spores when working with contaminated hides. There is no person- to-person transmission of inhalational anthrax.

Anthrax: Cutaneous

- Most common form (95%)
- Inoculation of spores under skin
- Incubation: one to 7 days
- Small papule --> ulcer surrounded by vesicles (24-28h)
- Painless eschar with edema
- Death 20% untreated; rare treated



USAMRICD

Michigan Department of Community Health

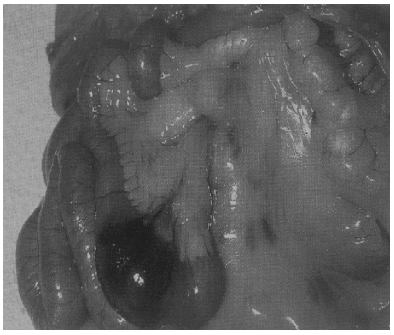
Cutaneous anthrax is the most common naturally occurring form of *B. anthracis* infection. Cutaneous anthrax is contracted when spores are inoculated under skin where there is a break such as a cut, there is no infection of intact skin.

Cutaneaous anthrax results in a painless non pyogenic ulcer with surrounding edema. Death occurs in approximately 20% of untreated cases but is very rare if treated with antibiotics.

(Picture of eschar with surrounding edema)

Anthrax: Gastrointestinal

- Ingestion of contaminated meat
- Incubation: two to 5 days
- Fever, acute gastroenteritis, vomiting, bloody diarrhea
- Intestinal eschar similar to cutaneous anthrax lesion
  - hemorrhagic
- Progression to generalized toxemia
- Mortality rate greater than 50% despite Rx



CDC

Michigan Department of Community Health

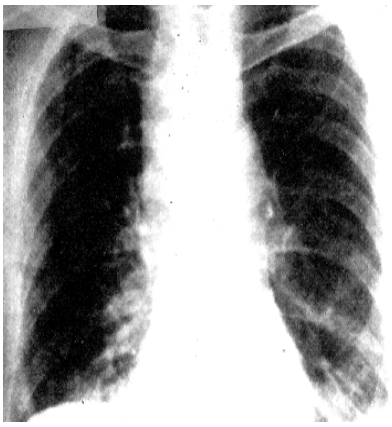
Gastrointestinal anthrax is very rare and results from ingesting contaminated meat. Diagnosis is difficult and the disease can result in high mortality despite treatment. Symptoms include acute gastroenteritis, bloody diarrhea, and an intestinal eschar

similar to a cutaneous anthrax lesion.

[Picture of intestinal lesion from GI anthrax]

Anthrax: Inhalational

- Inhalation of spores
- Incubation: 1 to 60 days
- Initial symptoms (2-5 d)
  - fever, cough, myalgia, malaise, chest pain, acute respiratory distress
- Terminal symptoms (1-2d)
  - High fever, dyspnea, cyanosis
  - hemorrhagic mediastinitis/effusion
  - Rapid progression shock/death
- Mortality rate ~ 100% despite aggressive Rx



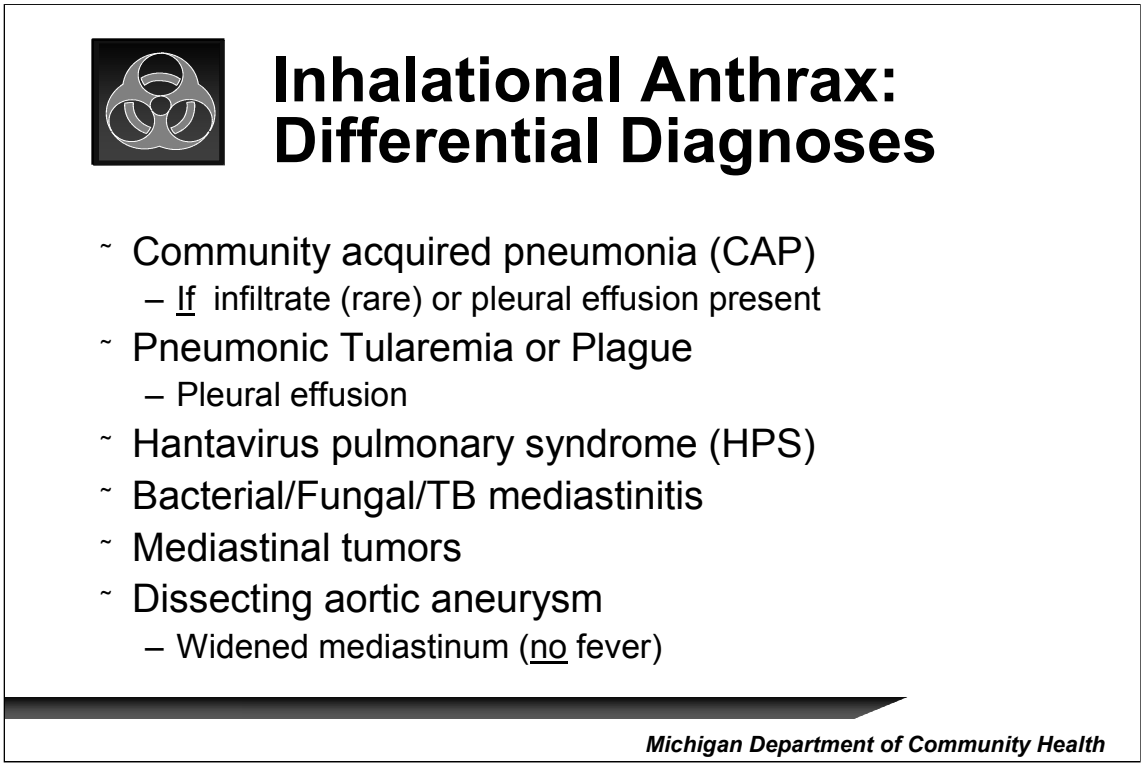
CDC

Michigan Department of Community Health

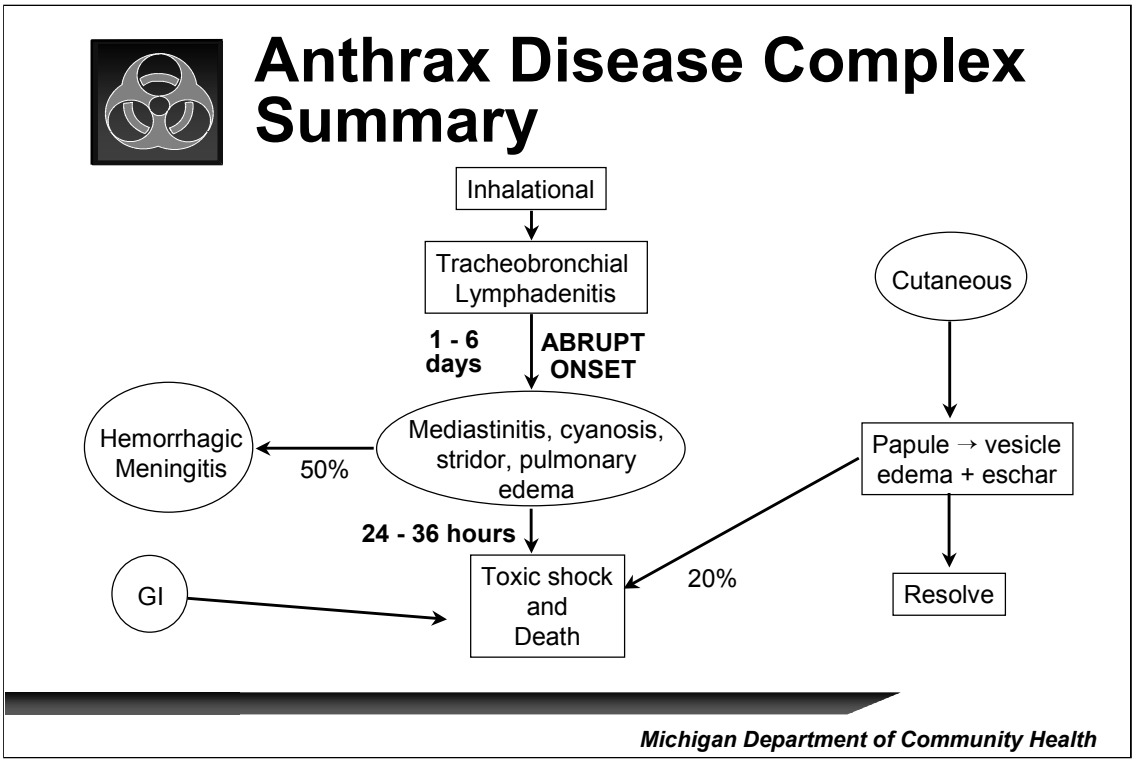
Inhalational anthrax is very rare but the most likely form of disease presentation in a bioterrorism event.

Incubation is usually 2-3 days but can be shorter or longer, up to as many as 60 days. Initially patients will present with flu-like symptoms, followed 1-2 days later by severe symptoms such as high fever, dyspnea, cyanosis, and hemorrhagic mediastinitis. Up to 50% of inhalational anthrax cases may also have hemorrhagic meningitis. Antibiotic treatment before onset of severe symptoms may prevent death, otherwise even with aggressive treatment mortality is near 100%.

[Picture of widened mediastinum representing hemorrhagic mediastinitis which is pathognomonic for inhalational anthrax]



Syptoms of inhalational anthrax are similar to severe community acquired pneumonia, but usually no infiltrate can be seen in inhalational anthrax. Inhalational anthrax is also similar to pneumonic tularemia or plague as pleural effusions can be seen in all 3 of these diseases. Other conditions to consider in the differential diagnosis are Hantavirus Pulmonary Syndrome , bacterial/fungal/TB mediastinitis, mediastinal tumors and a dissecting aortic aneurysm.



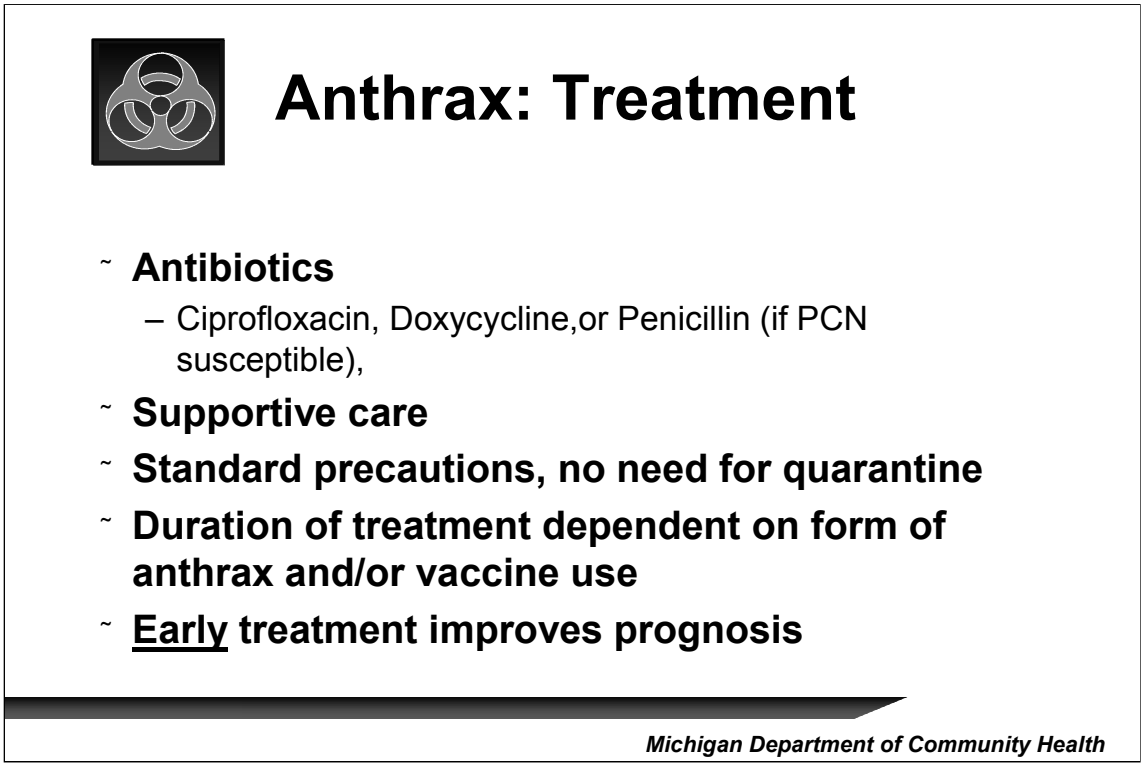
Aerosol exposure is the most likely scenario in a terrorist biological attack. Following the inhalation, alveolar macrophages engulf the spores, the bacteria become vegetative and are transported to the tracheobronchial nodes. Early symptoms are nonspecific: malaise, nonproductive cough, and/or chest discomfort.

Within 1 - 6 days of onset of symptoms, there is a sudden onset of respiratory distress, dyspnea, stridor, and cyanosis.

Tracheobronchial nodes undergo a necrotizing edematous lymphadenitis, progressing to a mediastinitis and pulmonary edema, with or without a bloody pleural effusion.

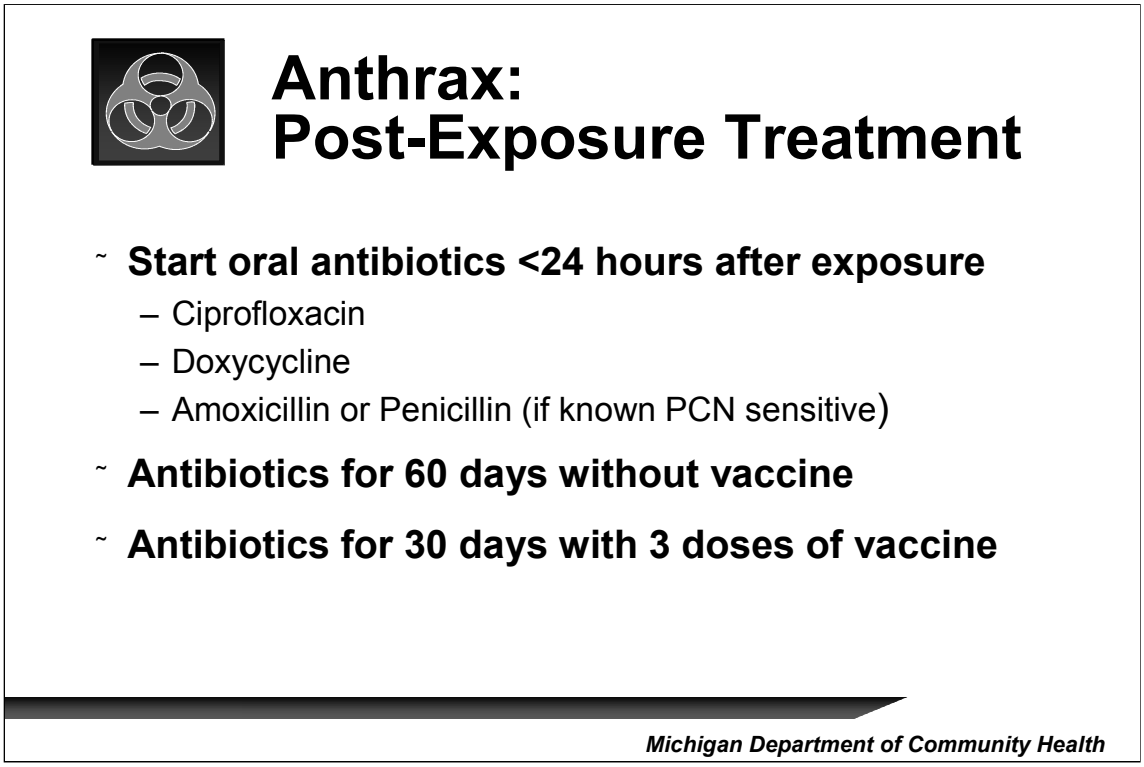
50 percent of cases may rapidly develop a concurrent hemorrhagic meningitis with bloody cerebral spinal fluid.

Septicemia, toxic shock, and death occur within an additional 24 to 36 hours.



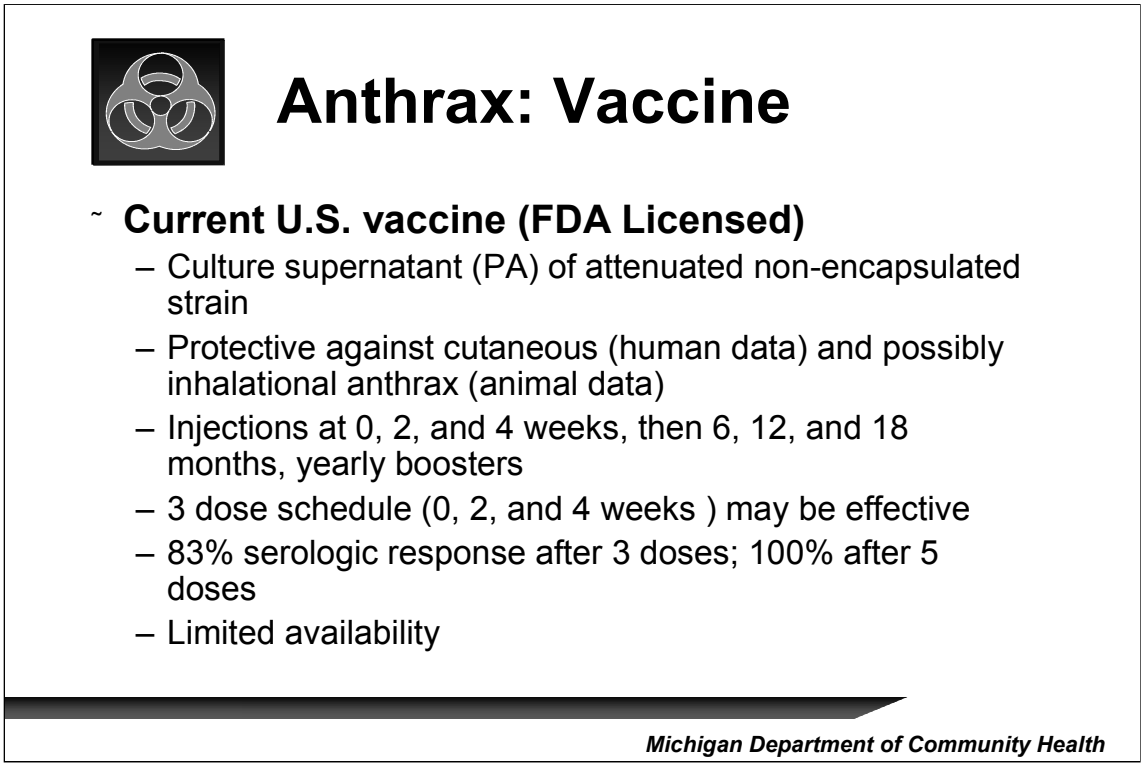
Early treatment is essential in treating anthrax as antibiotics will kill the organism but do not affect the toxin already released. Antibiotics used to treat anthrax are Penicillin, Doxycycline, or Ciprofloxacin. If the patient survives the initial illness, antibiotic therapy may be needed for as long as 30 to 60 days depending on the form of anthrax and/or vaccine use. It is important that health care providers use antibiotic susceptibility testing to help guide therapy.

Health care workers should use standard precautions when caring for patients infected with inhalational anthrax. Quarantine is not required as anthrax is not spread person to person.



Prophylaxis is most effective if given before the onset of symptoms or possibly before onset of severe symptoms. The length of treatment is dependent on concurrent vaccine use (if available); 60 days without vaccine and 30 days with 3 doses of vaccine. This recommendation is based on observations that inhaled spores may cause disease as long as 60 days post exposure.

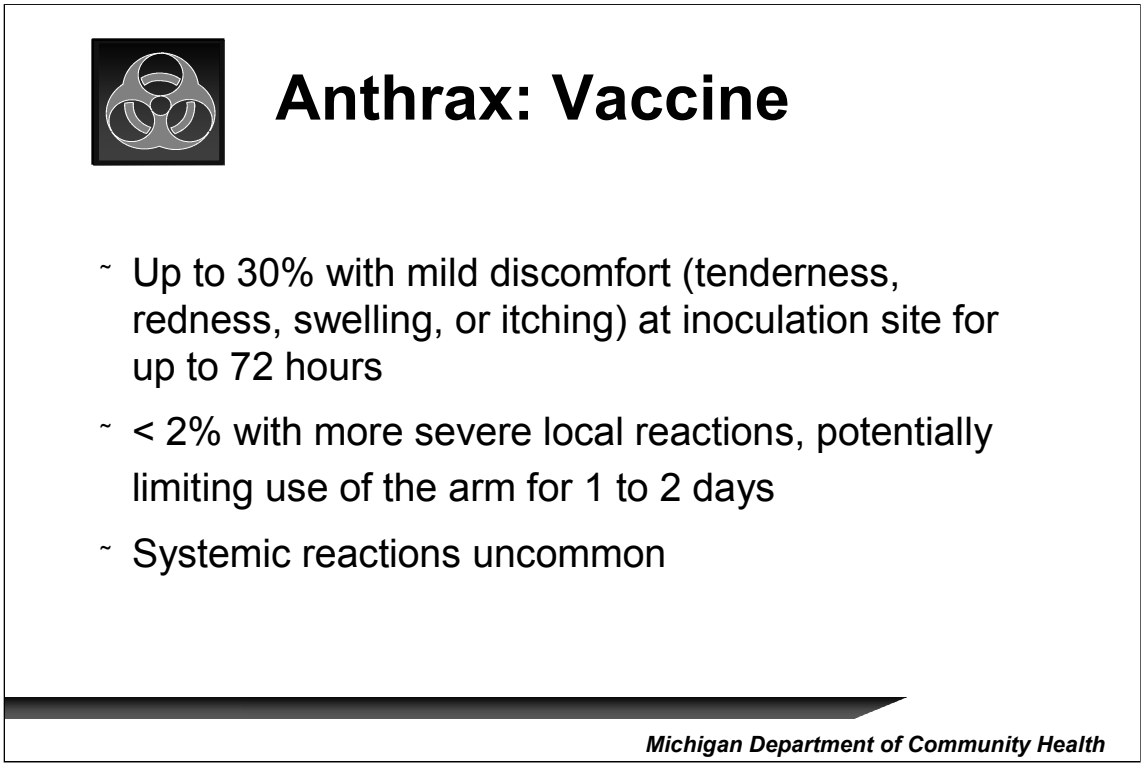
*These treatments are not generally recommended for women and children. Their use in a specific clinical setting must be decided upon the basis of their risk versus the benefit to the patient.



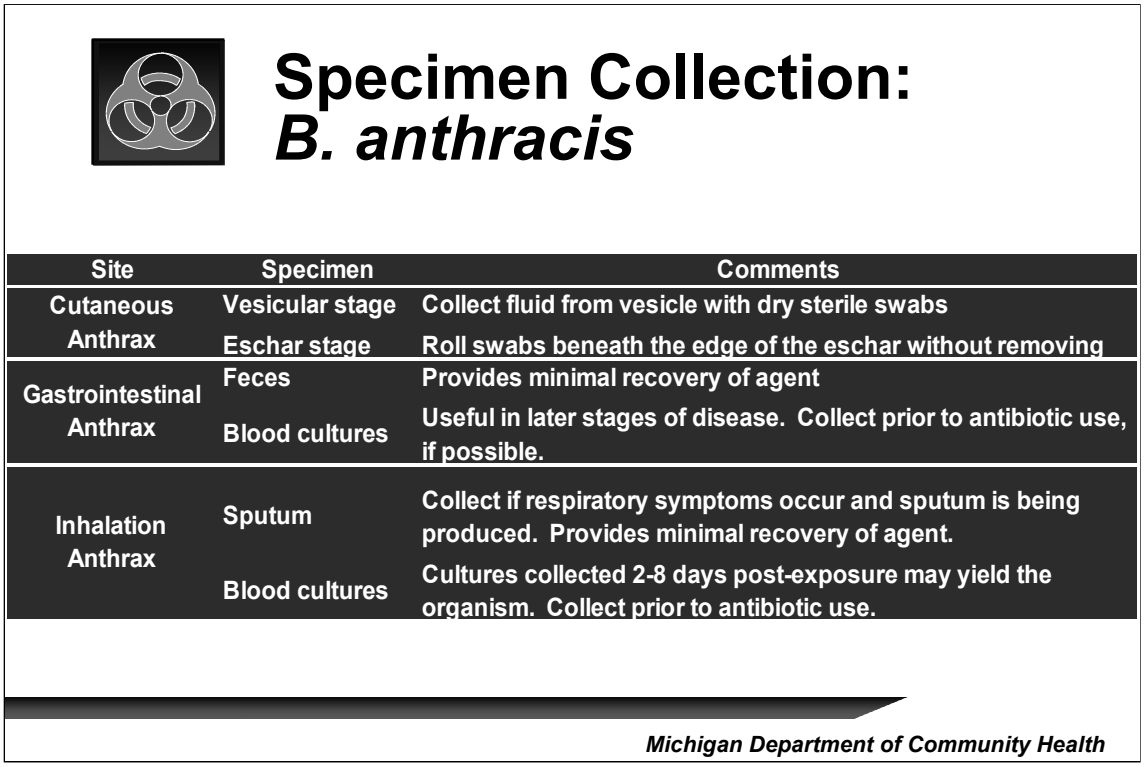
The anthrax vaccine currently licensed for use in the United States by the FDA is comprised of supernatant with Protective antigen and contains no live components. This vaccine has been shown to effective in protecting against the cutaneous form of anthrax in Humans and the inhalational form in animals. There is no data on the effectiveness of the vaccine against inhalational anthrax in humans.

The current initial pre-exposure series consists of 6 shots at 0, 2, and 4 weeks, and 6,12, and 18 months. This initial series is then followed by yearly boosters. A limited 3 dose schedule at 0, 2, and 4 weeks may be effective as there is 83% serologic response after these doses have been given.

Health care workers should be aware that there is limited availability of vaccine and it is not available to the general public.



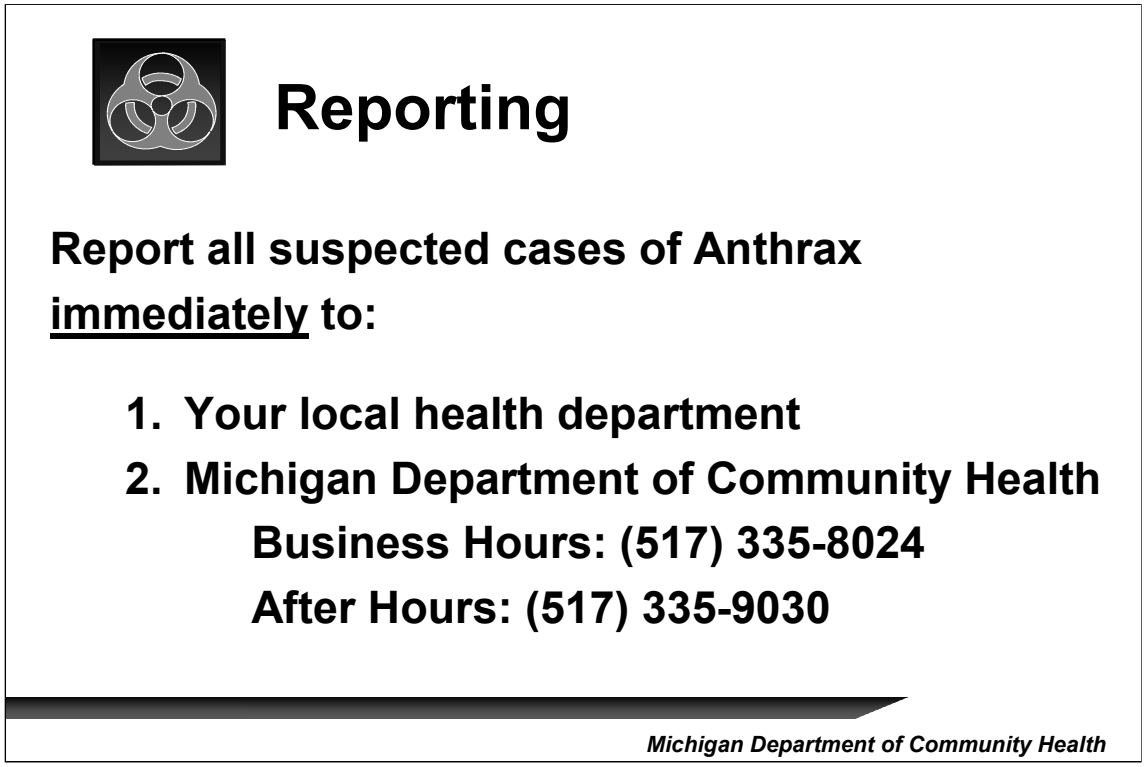
For those that do receive the vaccine, most reactions are local with up to 30% of the recipients reporting mild discomfort at the inoculation site for up to 72 hours. Less than 2% of those vaccinated have a more severe local reaction which would potentially limit the use of the arm for 1 to 2 days. Severe systemic reactions are uncommon following anthrax vaccination.



The chart above lists the specimens and information related to their collection when testing for infection with *B.anthracis*.

Specimens collected for *B. anthracis* must be submitted to the Michigan Department of Community Health Regional Laboratory System or the Michigan Department of Community Health. Contact your clinical laboratory for further information on testing prior to submission.

* Nasal Swabs: Culture of nasal swabs is used to detect anthrax spores. Nasal swabs can occasionally document exposure, but cannot rule out exposure to *B. anthracis*. As an adjunct to epidemiologic evaluations, nasal swabs may provide clues to help assess the exposure circumstances, but are **NOT** to be used diagnostically.

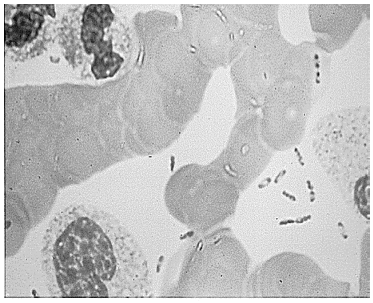


All suspected cases of Anthrax should be reported **immediately** to your local health department and the Michigan Department of Community Health at the phone numbers listed above.

For further information visit our website at www.MDCH.state.mi.us.

Plague: Overview

- **About 10-15 cases/year U.S.**
  - Mainly SW states
  - Bubonic most common form
- **Natural vector - Rodent flea**

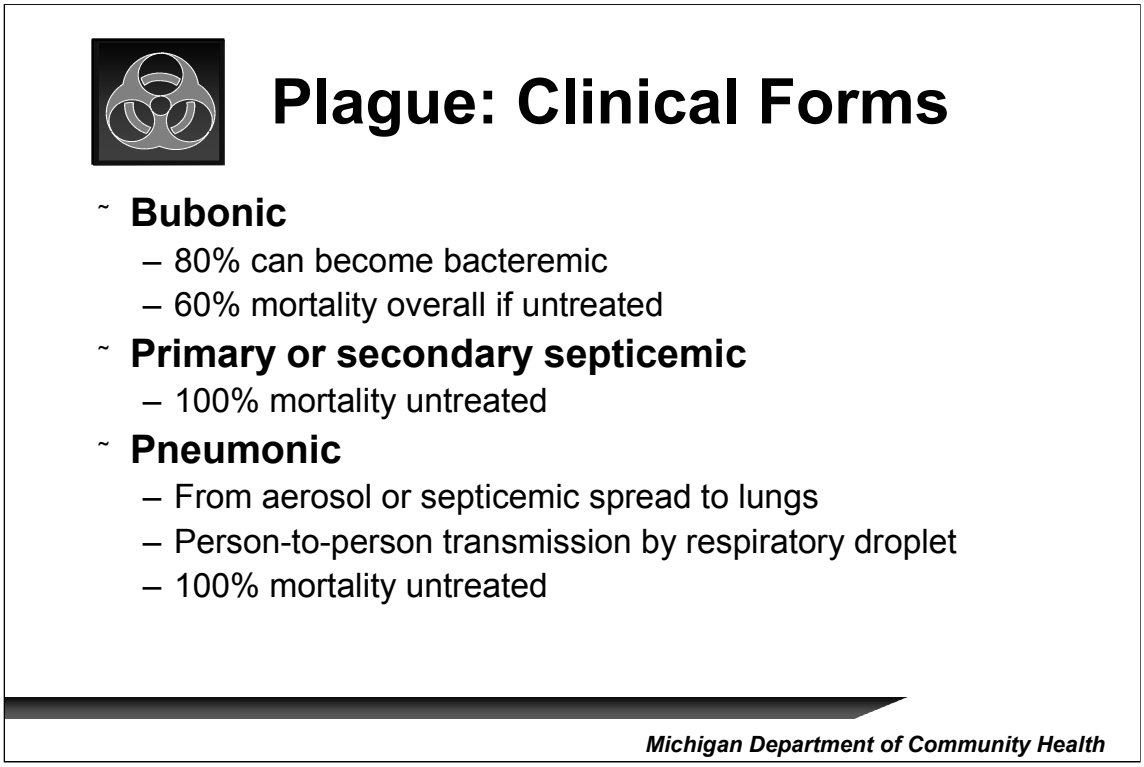


Michigan Department of Community Health

Plague is one of the few bioterrorist disease threats that occurs naturally in the United States. There are approximately 15-20 cases a year in the United States with most of those occurring in the southwest portion of the county. A case of Plague has never been reported in Michigan. Of the cases that do occur in the US, Bubonic is the most common form with only 1-2 cases a pneumonic plague occurring each year.

Yersinia Pestis, the causative agent of plague, is usually transmitted to humans by fleas from other mammalian hosts.

[Picture is Giemsa stain of *Y. pestis*]



Plague presents in three clinical forms: Bubonic, Primary Septicemic, and Pneumonic. Of these three forms, Bubonic is the most common presentation with swollen lymph nodes called buboes. Eighty percent of bubonic cases can become bacteremic with an overall mortality rate of 60% if left untreated. The Primary Septicemic form of plague will not result in buboes, but can lead to secondary pneumonia. Mortality of Primary Septicemic plague is 100% if left untreated. The third form of plague, Pneumonic, is primarily the result of aerosol infection or septicemic spread to the lungs and is the most likely form of plague to be seen in a bioterrorist event. Pneumonic plague can be spread person-to-person by respiratory droplet. Appropriate precautions should be taken. If left untreated, mortality of pneumonic plague is 100%.

Plague: Bubonic

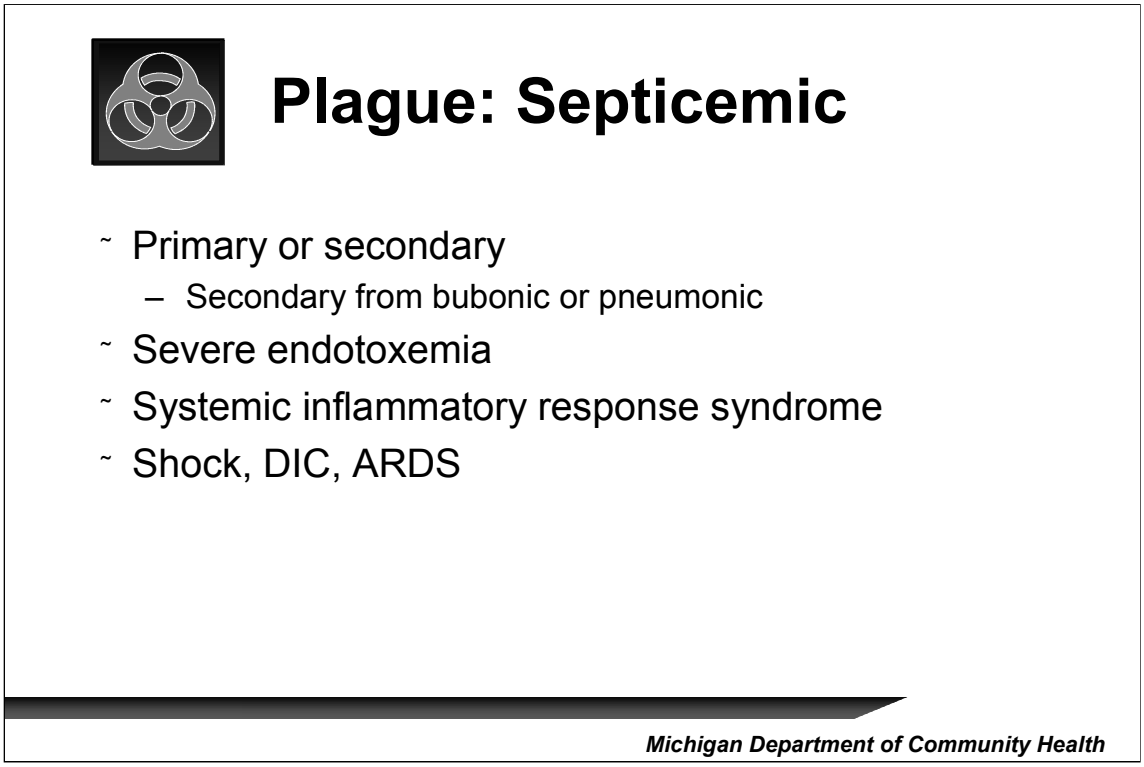
- **Incubation: 2-8 days**
- **Sudden onset fever, chills, weakness, tender LNs**
- **Regional lymphadenitis (Buboes):**
  - Inguinal, axillary, or cervical LN most common
- **Cutaneous findings**
  - possible papule, vesicle, or pustule at inoculation site
  - Purpuric lesions - late

Source: USAMRICD

Michigan Department of Community Health

Symptoms of bubonic plague typically develop 2 to 8 days after being bitten by an infected flea. These include fever, chills, weakness, and tender lymph nodes. Bubonic plague results in regional lymphadenitis which is most commonly found in the inguinal, axillary or cervical regions. Bubonic plague is also indicated by cutaneous findings that may include papules, vesicles or pustules at the inoculation site.

[Picture of swollen lymph nodes or buboes]

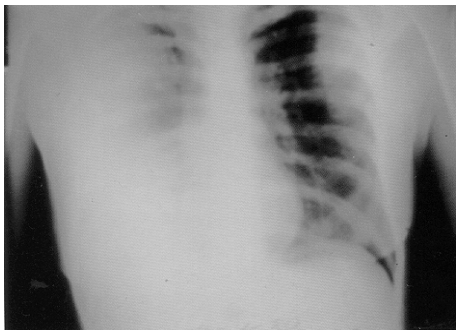


Septicemic Plague is a rare event and can be either a primary event or secondary to bacteremia and sepsis from bubonic or pneumonic plague. This form of plague is associated with severe endotoxemia and systemic inflammatory response.

Patients develop shock, disseminated intravascular coagulopathies, and adult respiratory distress syndrome. Thrombosis in small blood vessels can lead to gangrene of peripheral areas such as nose, fingers, toes, etc. This is seen in the later stages of the disease and should not be used for diagnosis of the disease to initiate early lifesaving treatment.

Plague: Pneumonic

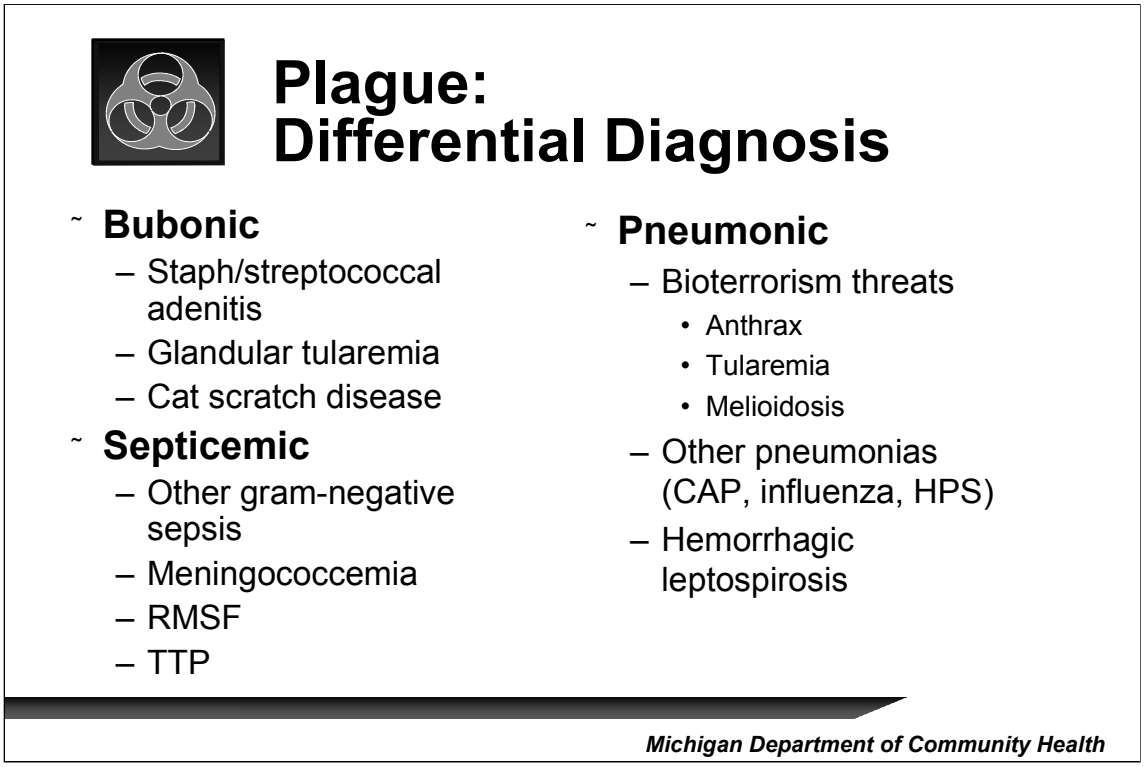
- Incubation: 1-3 days
- Sudden onset headache, malaise, fever, myalgia, cough
- Pneumonia progresses rapidly to dyspnea, cyanosis, hemoptysis
- Death from respiratory collapse/sepsis



Source: USAMRICD

Michigan Department of Community Health

Pneumonic plague is rare, usually only 1-2 cases/year in US, and is characterized by a rapid onset of symptoms including high fever and hemoptysis.The disease progresses rapidly and will result in death from respiratory collapse/sepsis if not treated early.



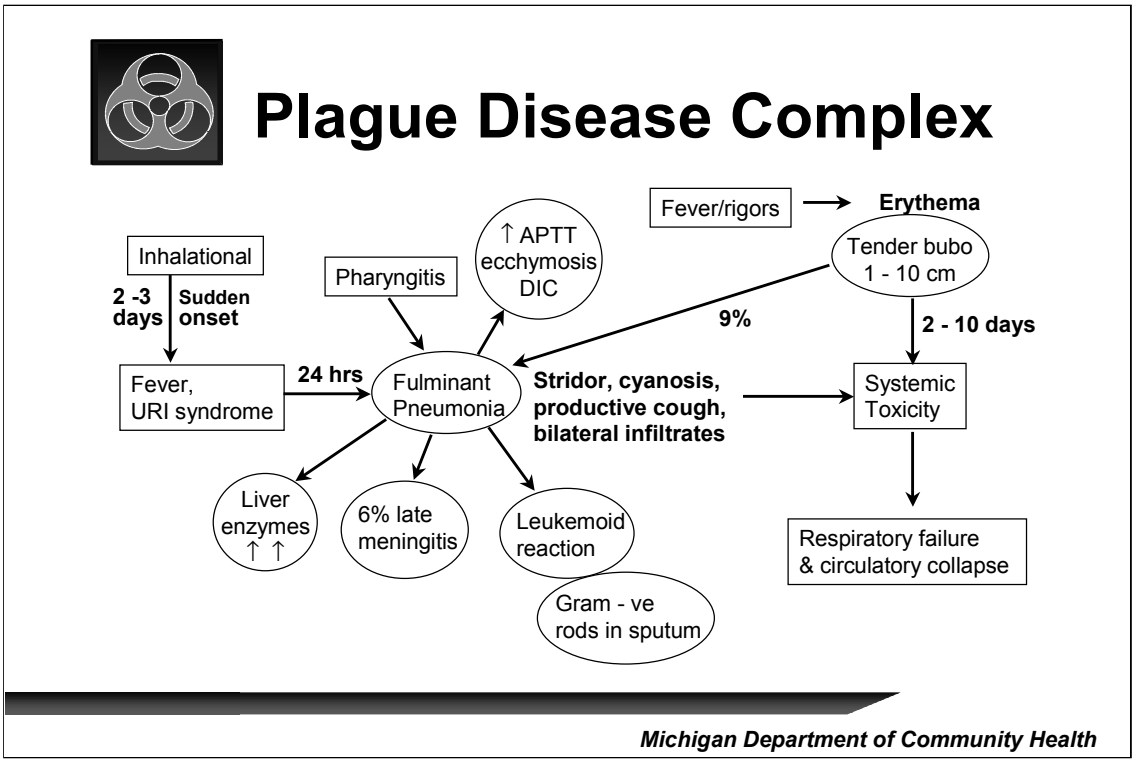
The chart above lists several differential diagnoses for each clinical form of plague. Listings of associated abbreviations can be found below.

RMSF = Rocky Mountain Spotted fever

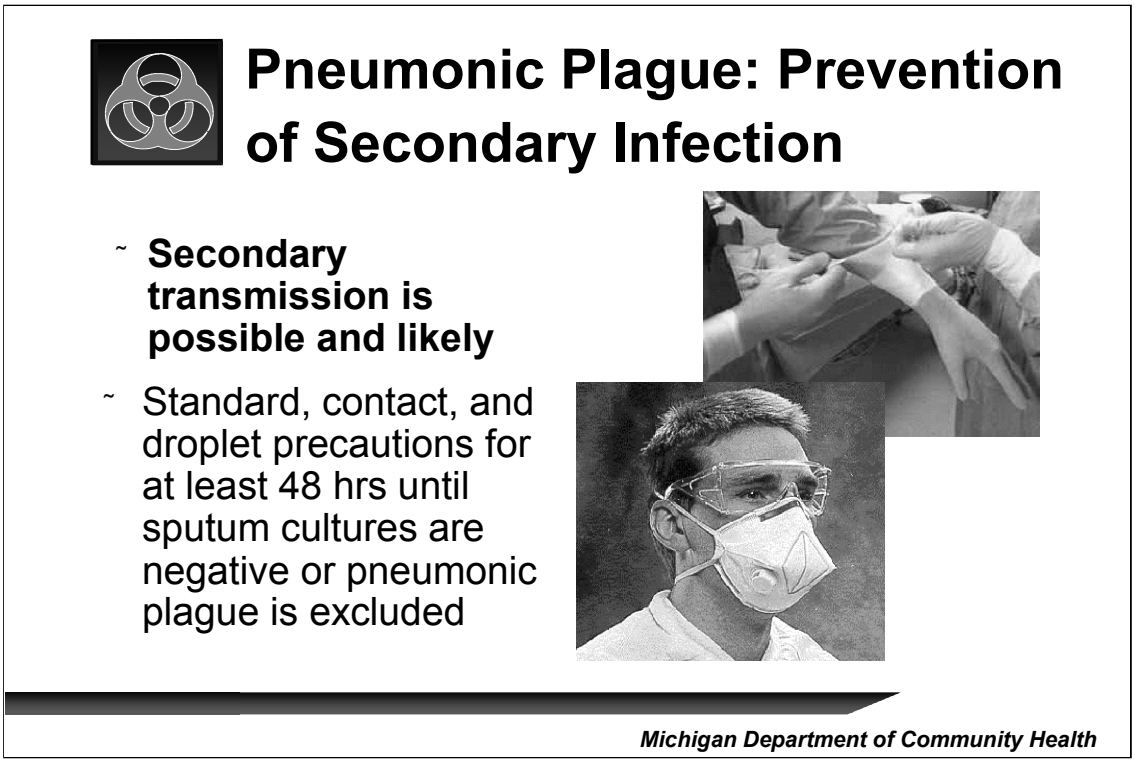
TTP= thrombotic thrombocytopenic purpura

HPS= Hantavirus pulmonary syndrome

CAP= community acquired pneumonia

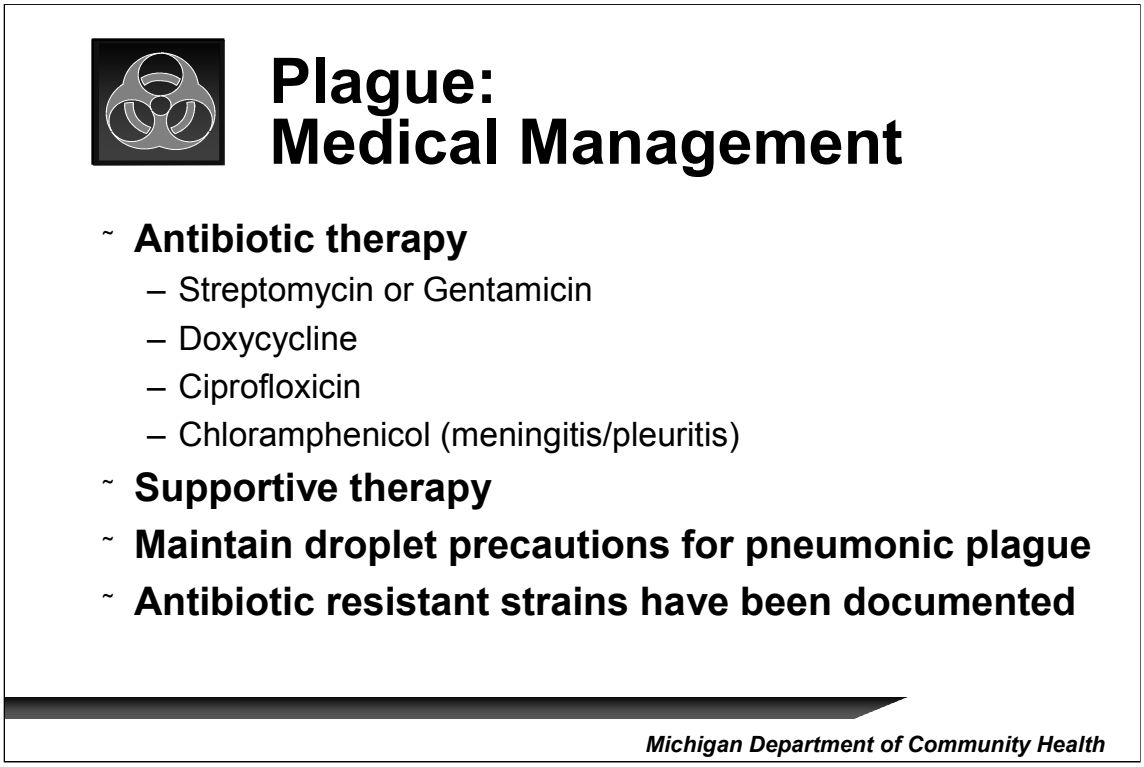


Pneumonic plague presents within 2 to 3 days of aerosol inhalation of bacilli (from biological weapon agent dissemination source or from respiratory droplets from another infected patient). There is a sudden onset of fever, chills, and an influenza-like syndrome followed within 24 hours by the onset of a fulminant pneumonia with hepatocellular damage and systemic toxicity. Coagulation abnormalities are common and severe ecchymosis may occur ("black death"). Oropharangeal primary infections may progress to fulminant pneumonia following endeobronchial aspiration of plague bacilli. This fulminant pneumonia is rapidly followed by systemic toxicity, respiratory failure, and circulatory collapse. Six percent of pneumonia cases have an accompanying meningitis.



Pneumonic plague may be highly communicable under appropriate climate conditions. For patients with confirmed pneumonic plague, droplet precautions are required until sputum cultures are negative. This category of personal protection requires a surgical mask and suggests a private room. However, patients may be cohorted or, if necessary, placed in a room where they are separated by several feet.

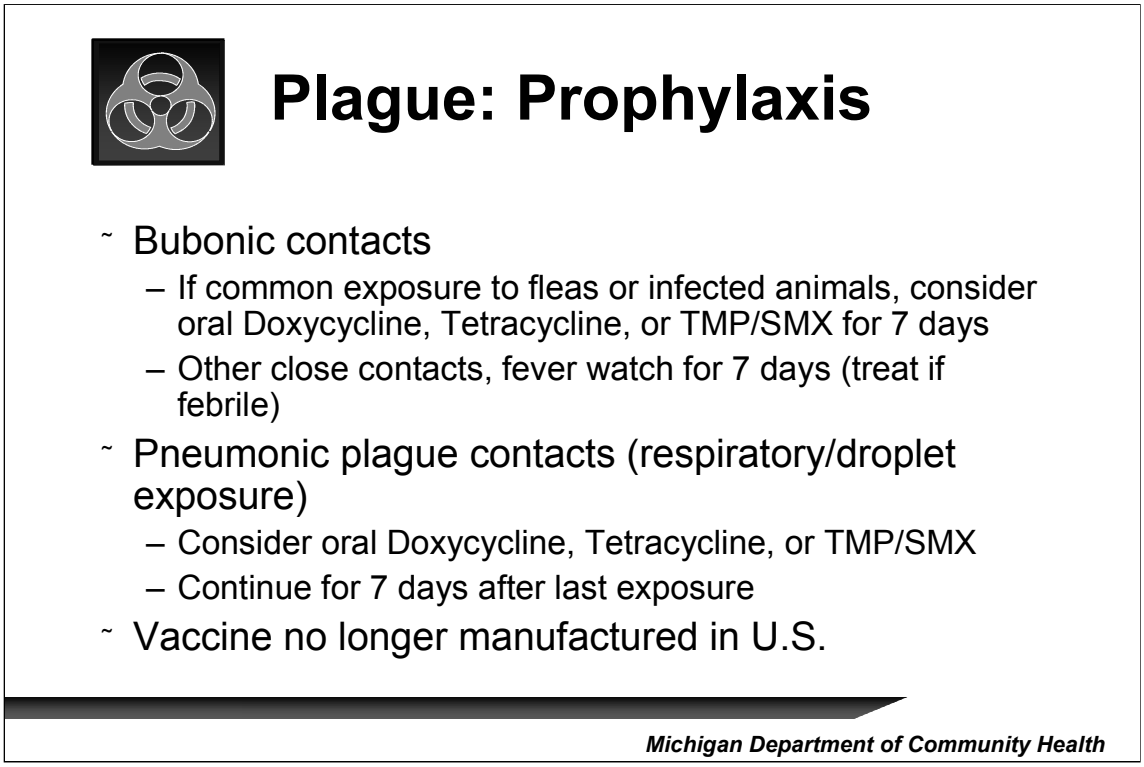
Accidental exposures to health care workers are managed by giving post-exposure tetracycline or doxycycline therapy for a minimum of 7 days. Vaccine is ineffective against aerosol exposures to plague.



Early antibiotic therapy of plague patients is imperative. Streptomycin and Gentamicin are considered the drugs of choice but supplies could be quickly exhausted in a mass casualty incident. Alternative choices include doxycycline, ciprofloxicin, and chloramphenicol. In addition to antibiotic therapy, many patients will also require advanced medical supportive therapy.

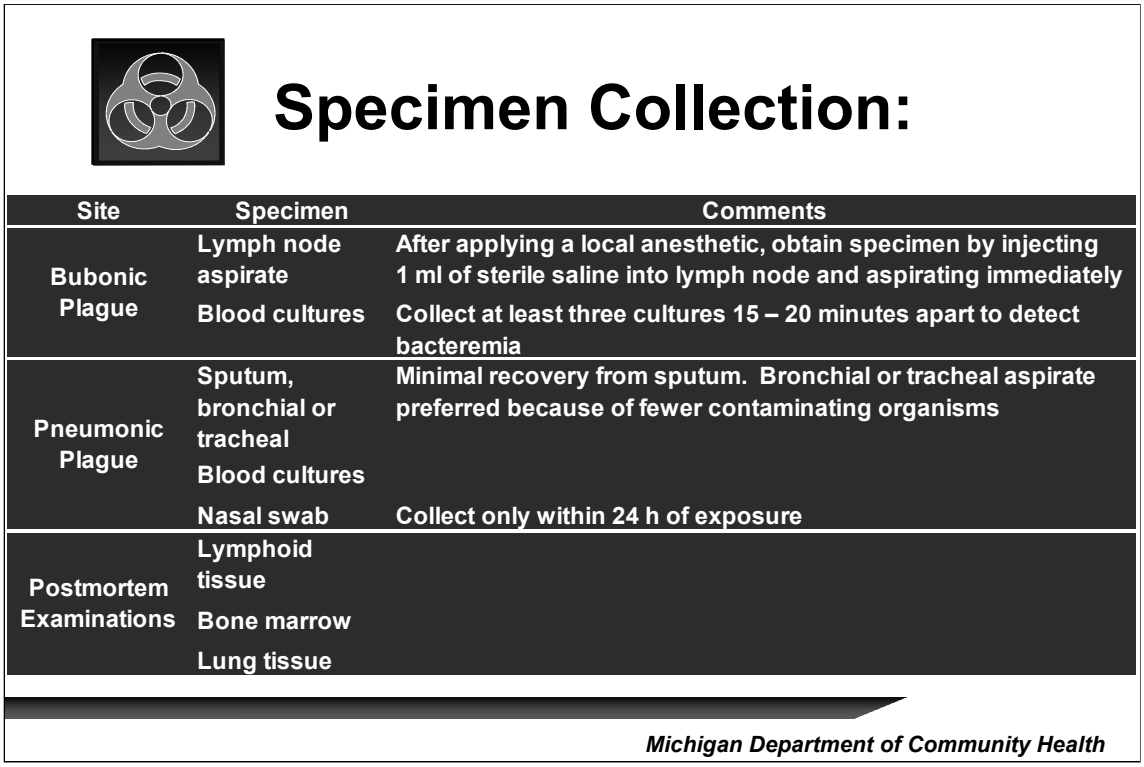
Patients with pneumonic plague should be considered infectious until 1) minimum of 48 hours after the initiation of appropriate antibiotic treatment with patient showing a favorable clinical response, i.e. no fever or 2) until one sputum culture is negative (at least 48 hours after start of therapy).

* These treatments are not generally recommended for women and children. Their use in a specific clinical setting must be decided upon the basis of their risk versus the benefit to the patient.



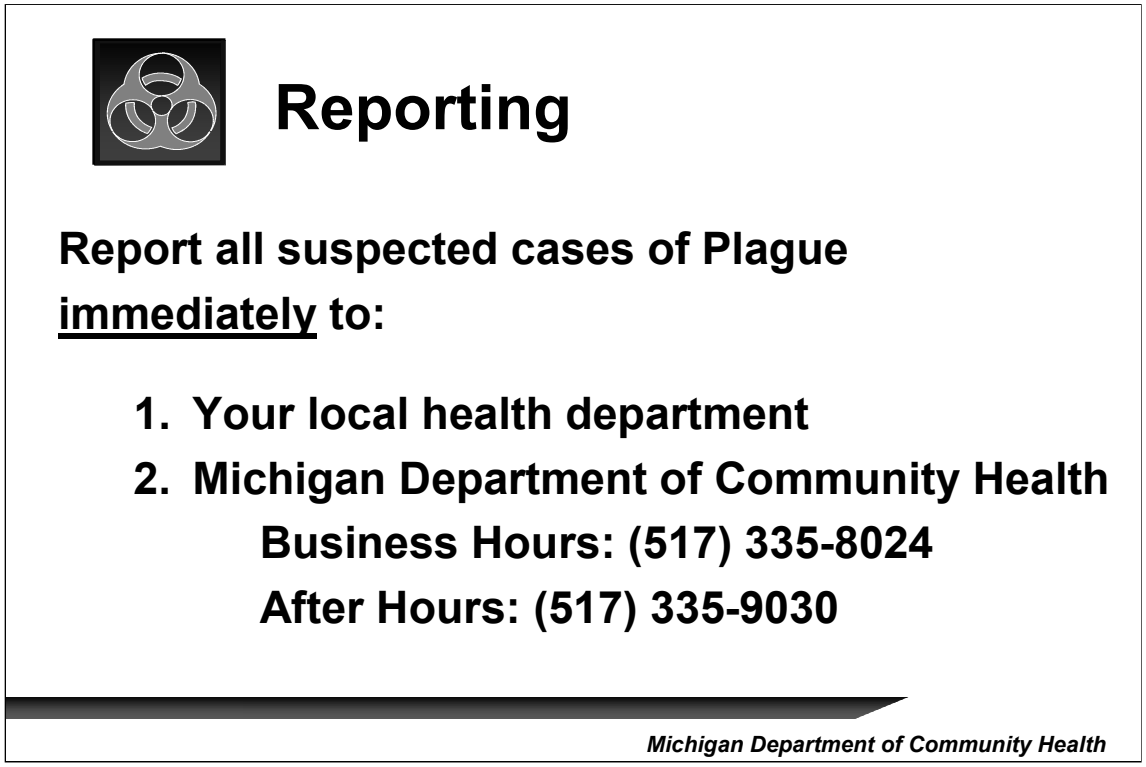
Prophylaxis should be given to contacts of patients with bubonic plague who have a common exposure to fleas or infected animals. Face to face contacts of pneumonic plague cases should be considered for prophylaxis with oral tetracycline or doxyclycline for 7 days after their last contact.

The vaccine for *Y. pestis* is a killed vaccine used by laboratory personnel working with large quantities of the organism, not routine clinical labs. It provides protection against the bubonic form, probably not protective against pneumonic.



The chart above lists the specimens and information related to their collection when testing for infection with *Y. Pestis*.

Specimens collected for *Y. Pestis* must be submitted to the Michigan Department of Community Health Regional Laboratory System or the Michigan Department of Community Health. Contact the Bureau of Laboratories (517-335-8063) for further information on testing prior to submission.



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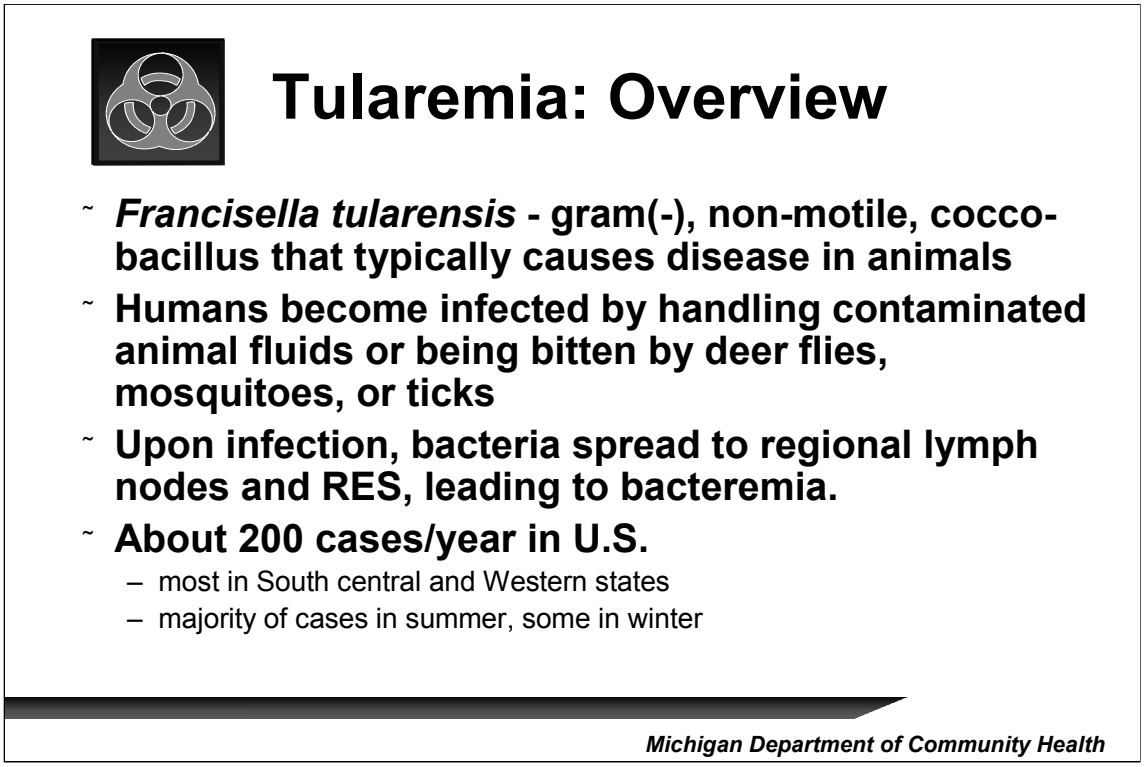
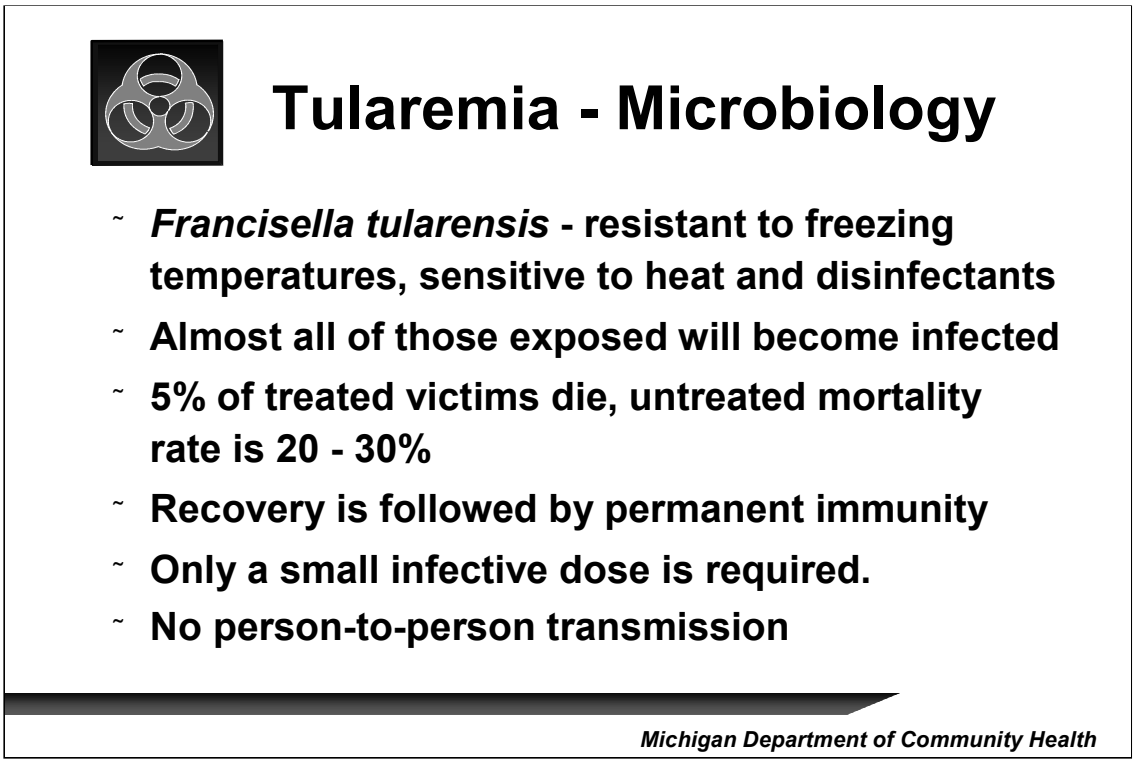


Francisella tularensis is a non-motile, gram-negative cocco-bacillus that typically causes disease in animals (rabbit fever, deer fly fever). It was discovered in 1911, in Tulare County, California. Humans can become infected by either handling diseased animal fluids or by being bitten by infected deer flies, mosquitoes, or ticks. Spores are not formed, but the organism can remain viable for weeks in a number of mediums and can be easily spread by aerosol. After infection occurs, the bacteria spread to regional lymph nodes and the reticuloendothelial system (RES), leading to bacteremia with secondary spread to the lungs and other organs.

Commonly known as "rabbit fever," hundreds of thousands of naturally acquired cases of Tularemia were documented during World War II. During the early period of biological warfare development, the organism was proven to be a serious and versatile for the former U.S. and Soviet BW programs. The bacterium could be disseminated as either a wet agent or dry powder, and with the appropriate stabilizers could effect a large area in an attack similar to the release of Anthrax spores. This was documented on numerous occasions by open air tests using nonpathogenic strains of the *Serratia marcesens* bacterium as a Tularemia simulant. Antibiotic resistant strains of Tularemia were developed by both the United States and Soviet Union. It is one of the few BW agents in which live agent aerosol experiments were conducted on human volunteers who were subsequently treated with antibiotics.

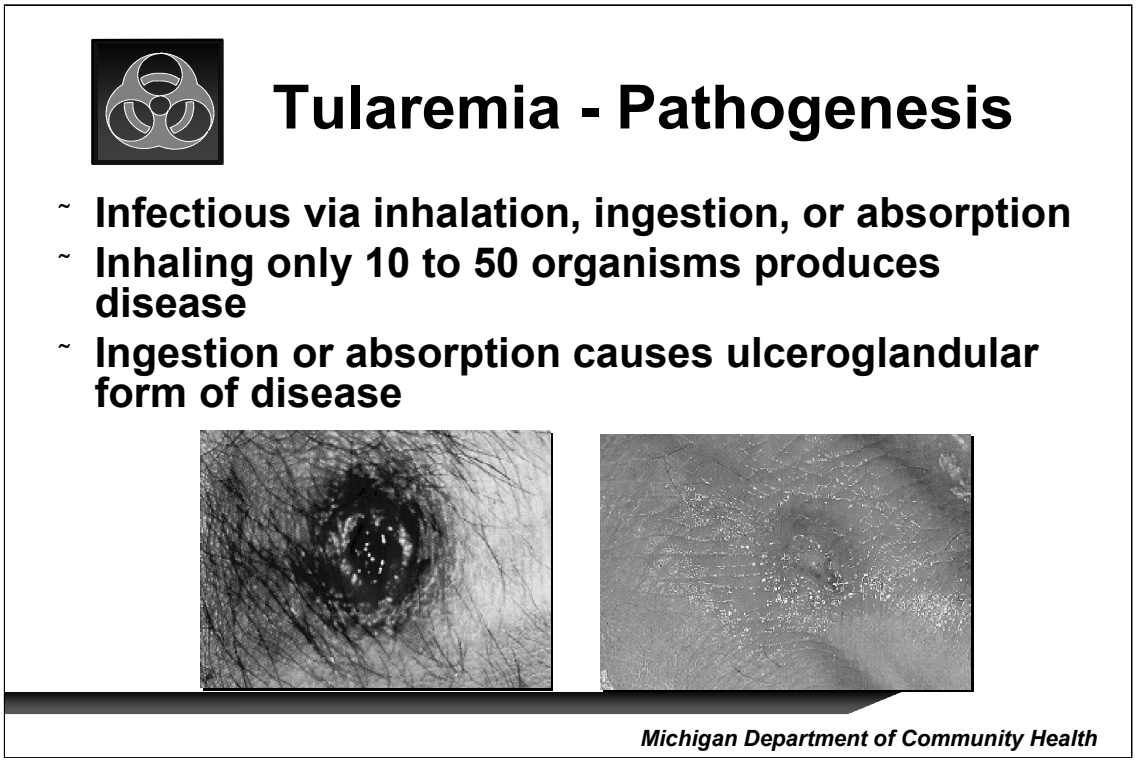
Approximately 200 cases occur every year in the United states. Most of these cases occur in the summer and are associated with bites from infected ticks. The remainder of the cases are mostly seen in winter and are associated skinning infected rabbits and hares.



F. tularensis is resistant for months to freezing temperatures, but is easily killed by heat and disinfectants. Almost 100 percent of those exposed to tularemia will become infected, but only about 5 percent of treated victims from the naturally occurring disease die. The case fatality rate with all forms of untreated typhoidal disease is approximately 35 percent, with 25 to 30 percent of untreated tularemia proving lethal. Recovery is followed by permanent immunity.

F. Tularensis is highly infective, and requires as little as ten organisms to cause infection.

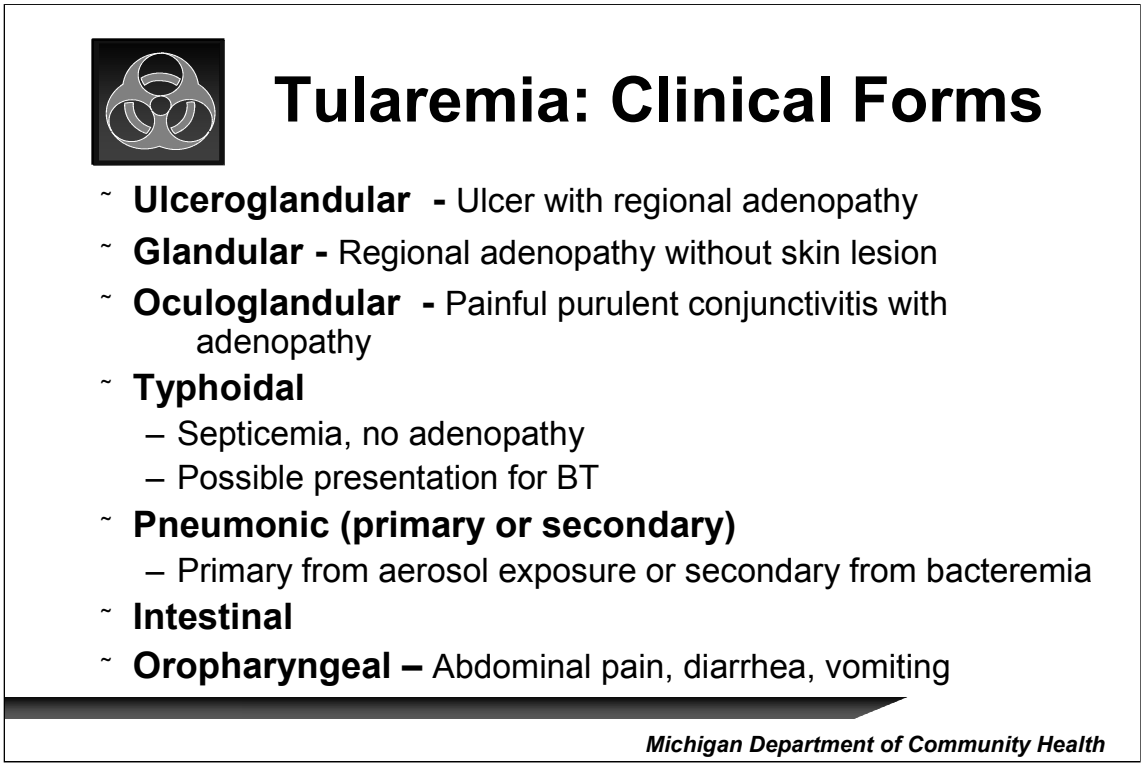
There is no person-to-person transmission of tularemia.



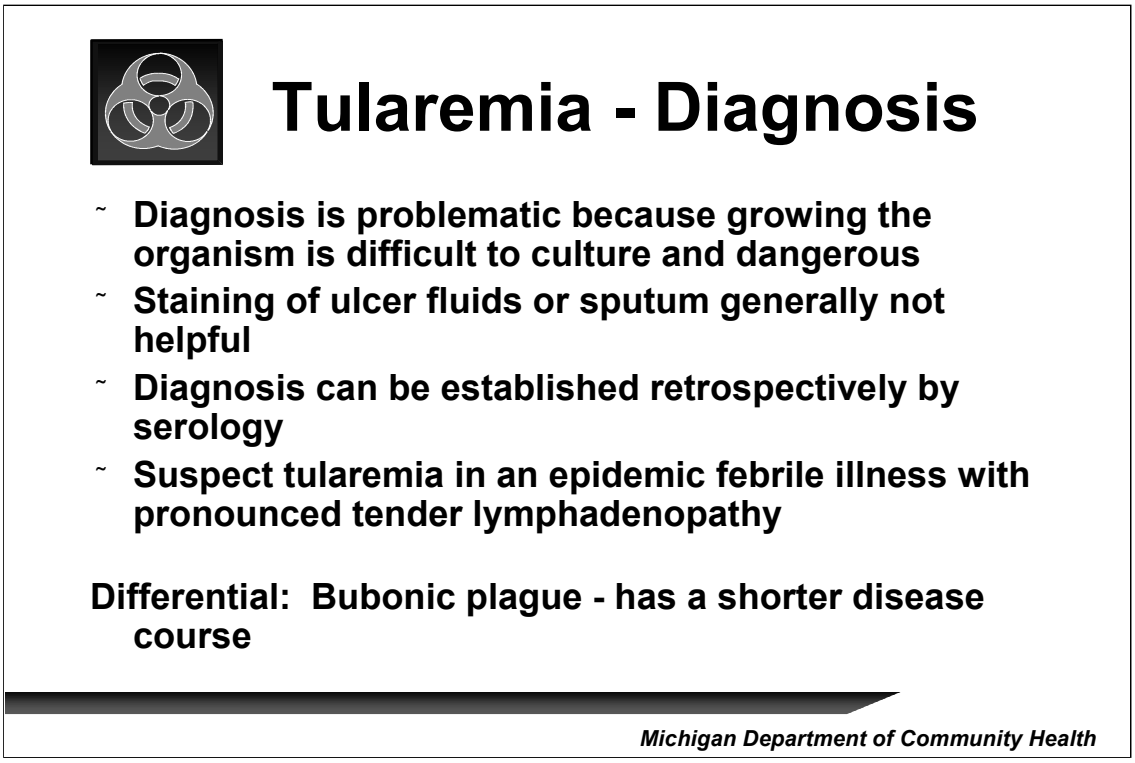
Tularemia occurs in many forms, but inhaling as few as 10 to 50 organisms will cause disease verses the 100 million organisms that need to be ingested to produce disease. Inhalation is the most deadly route of exposure. Inoculation, through minor skin lesions or arthropod bites, results in the ulceroglandular form of the disease pictured here.

The organism is rapidly engulfed by tissue macrophages where it causes local tissue destruction and inflammation. The organisms are then carried to the regional lymph nodes. Secondary spread to the lung and other organs can occur from a primary cutaneous infection.

Human aerosol studies suggest that an incubation period of 3 to 5 days would follow a covert aerosol release. This would be followed by the abrupt onset of fever, chills, headaches, non-specific myalgia and an initial non-productive cough. Untreated, this can progress into extensive lung damage with alveolar septal necrosis, parenchymal cavitation, and significant mortality with the more aggressive strains of the organism.



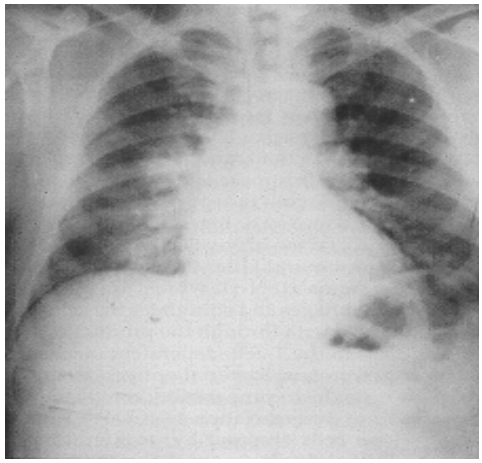
Tularemia can present as any one of the the following clinical forms, ulceroglandular, glandular, oculoglandular, typhoidal, pneumonic, intestinal, and oropharyngeal. Of these forms Ulceroglandular or glandular are the most common types comprising approximately 80% of infections. The forms most likely to be seen as a result of a bioterrorist event are the Primary pneumonic or Typhoidal forms



Confirmation of the diagnosis is problematic since growing the organism in culture is difficult and hazardous to laboratory personnel. Staining of ulcer fluids or sputum is also generally not helpful. Diagnosis can be established retrospectively by serology.

Tularemia: Pneumonic

- Incubation: 3 to 5 days (range 1-21 days)
- Abrupt onset fever, chills, headaches, myalgia, non-productive cough
- Segmental/lobar infiltrates, hilar adenopathy, effusions
- Mortality 30% untreated; < 10% treated



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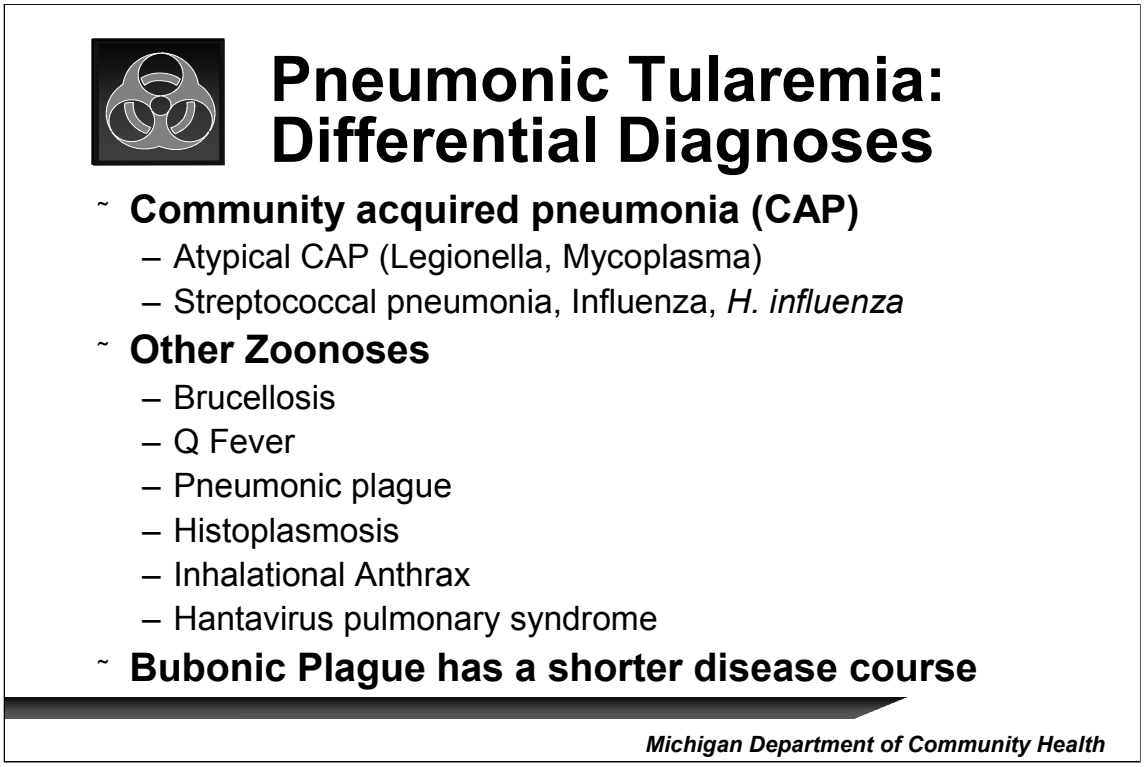
With Pneumonic Tularemia illness usually develops 3-5 days after exposure but can take as long as 21 days. The disease is characterized by fevers, chills, pulmonary infiltrates, and non-productive cough. The mortality from Tularemia is less than 10% If treated promptly but climbs to around 30% if not treated appropriately.



The Differential Diagnosis for Tularemia includes the following:

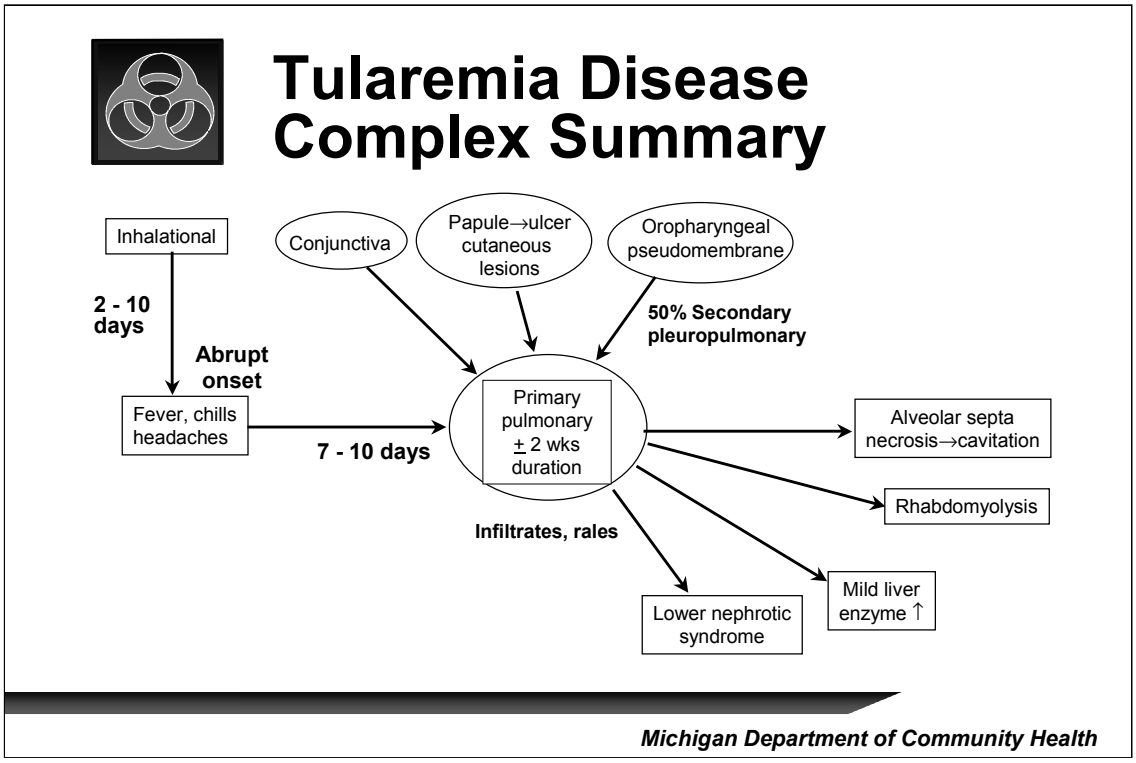
Community acquired pneumonias

atypical - Mycoplasma, Chlamydia, Legionella, etc.

Other less typical diseases with fever and/or pneumonic infiltrates

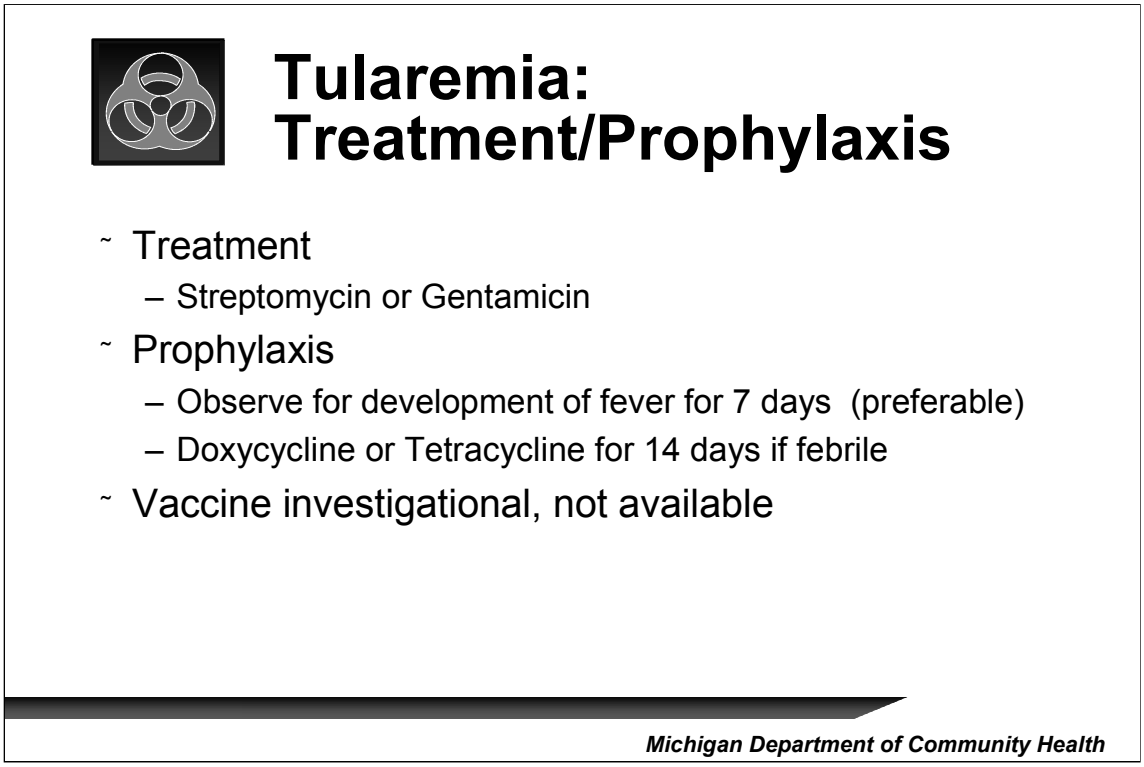
Other Zoonoses such as brucellosis, Q fever, Pneumonic plague, Histoplasmosis, Inhalational Anthrax, and Hantavirus pulmonary syndrome

Pneumonic Tularemia must also be differentiated from Bubonic plague, which has a shorter disease course, and from early inhalational anthrax, in the case of a bioterrorism scenario.



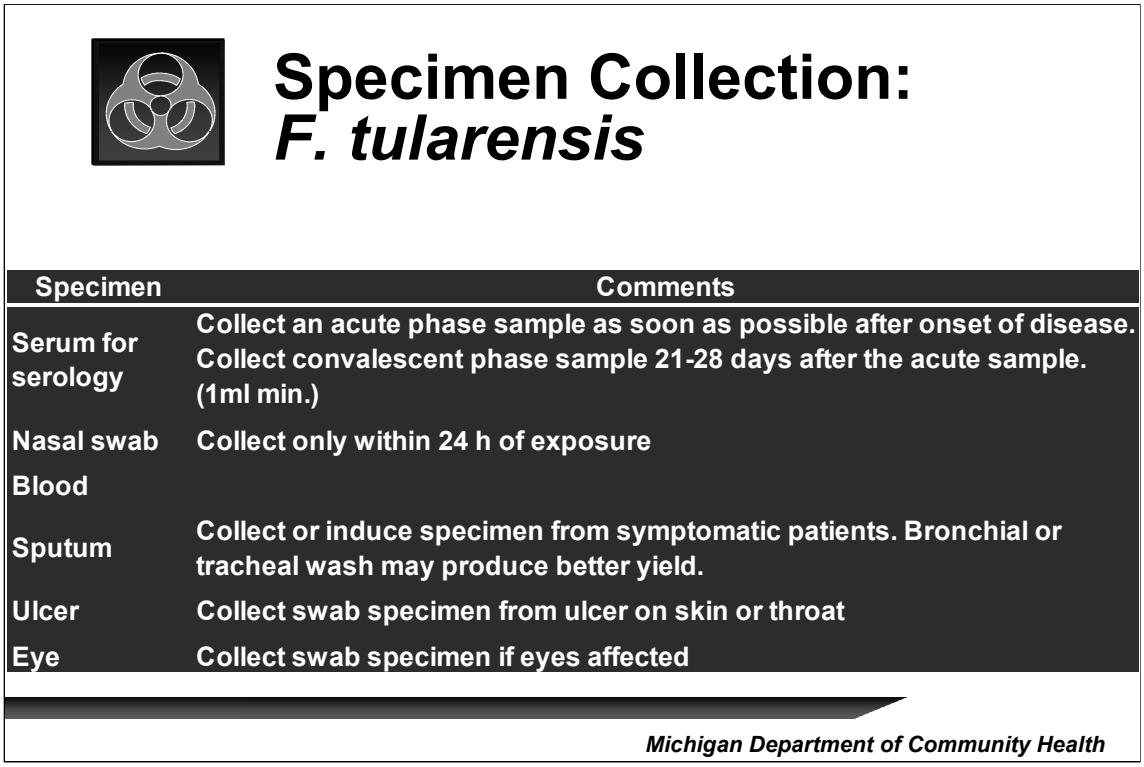
Tularemia is a disease marked by inflammation and necrosis which may occur, singularly or in combination, in the lung, oropharynx, eye, skin, and lymph nodes.

The disease progresses over 7 to 14 days. Inhalational tularemia is characterized by necrosis of the alveolar septa and regional nodes. 50 percent of patients initially presenting with cutaneous ulcers will progress on into a secondary pleuropulmonary infection. Long term complications may include hepatitis and renal damage.



The treatment recommendation for Tularemia is the administration of streptomycin or gentamicin. When considering prophylaxis, observation for development of fever over a period of 7 days is preferred. For a febrile patient, doxycycline or tetracycline administered for 14 days is the preferred method of prophylaxis. An investigational vaccine (more effective against aerosol challenge than in preventing ulceroglandualr form) is available in the US for laboratory personnel working routinely with *F. tularensis*; its possible role in post-exposure prophylaxis is not yet established.

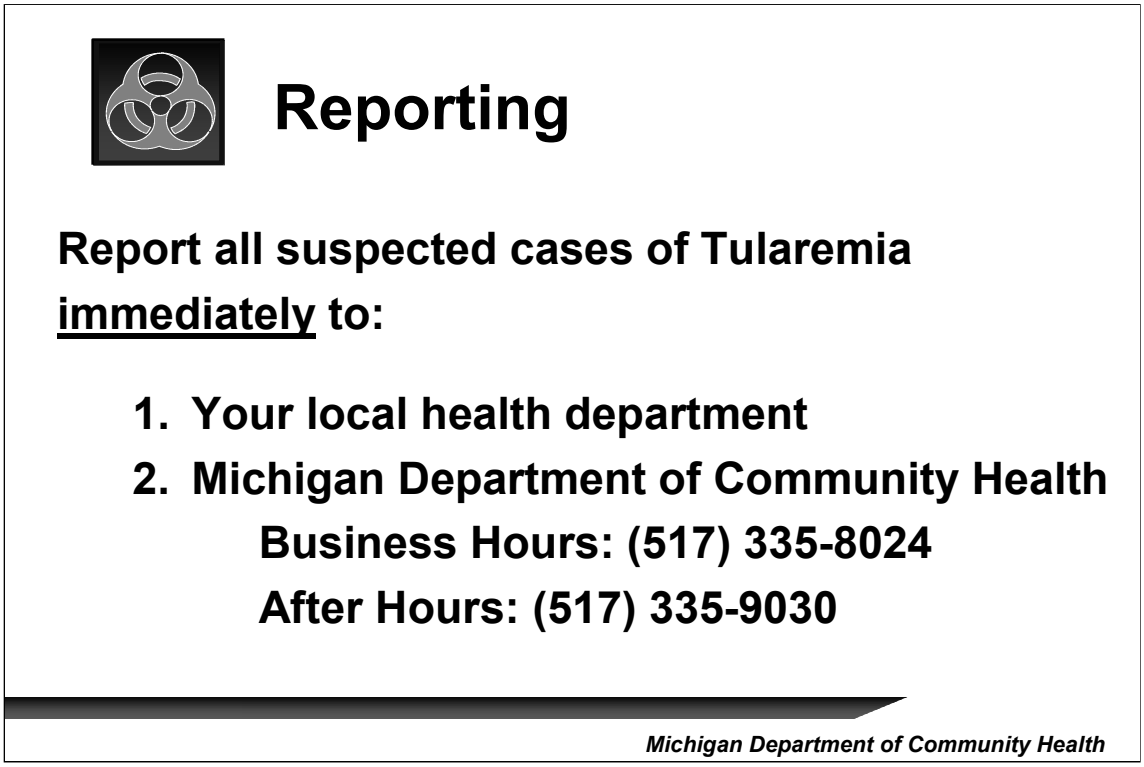
*These treatments are not generally recommended for women and children. Their use in a specific clinical setting must be decided upon the basis of their risk versus the benefit to the patient.



The chart above lists the specimens and information related to their collection when testing for infection with *F. tularensis*.

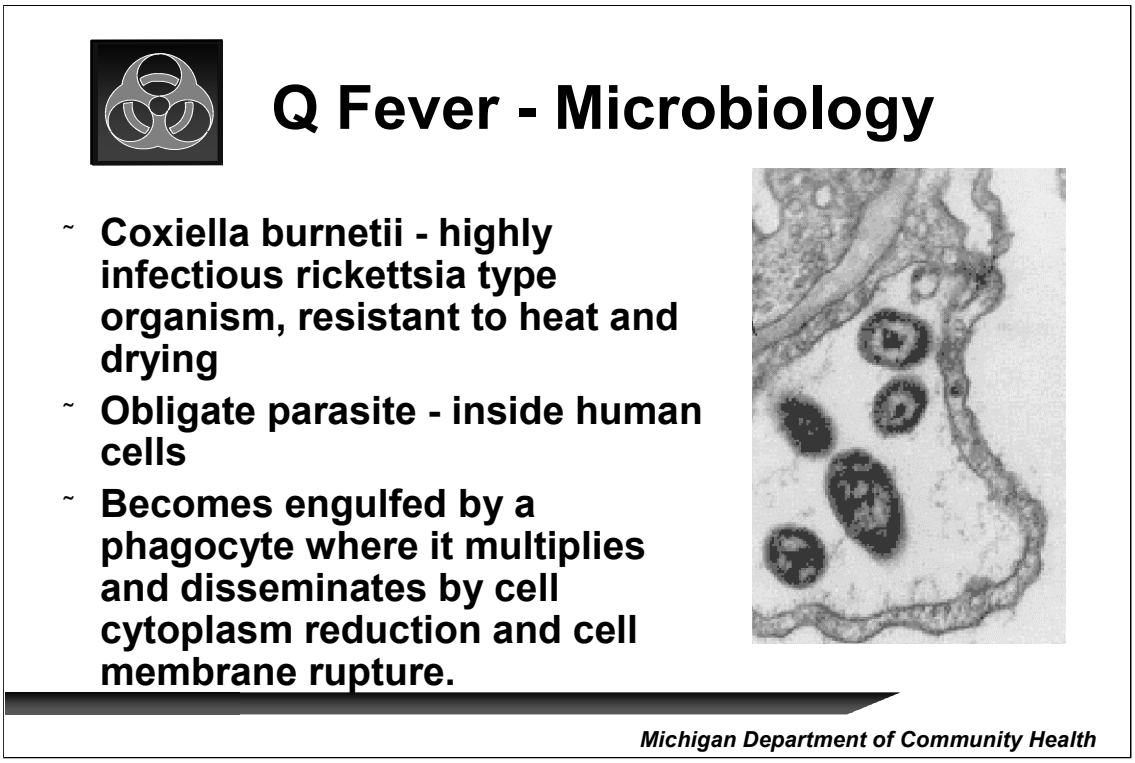
Samples should be stored and shipped frozen or preserved with merthiolate.

Specimens collected for *F. tularensis* must be submitted to the Michigan Department of Community Health Regional Laboratory System or the Michigan Department of Community Health. Contact the Bureau of Laboratories (517-335-8063) for further information on testing prior to submission.



All suspected cases of Tularemia should be reported **immediately** to your local health department and the Michigan Department of Community Health at the phone numbers listed above.

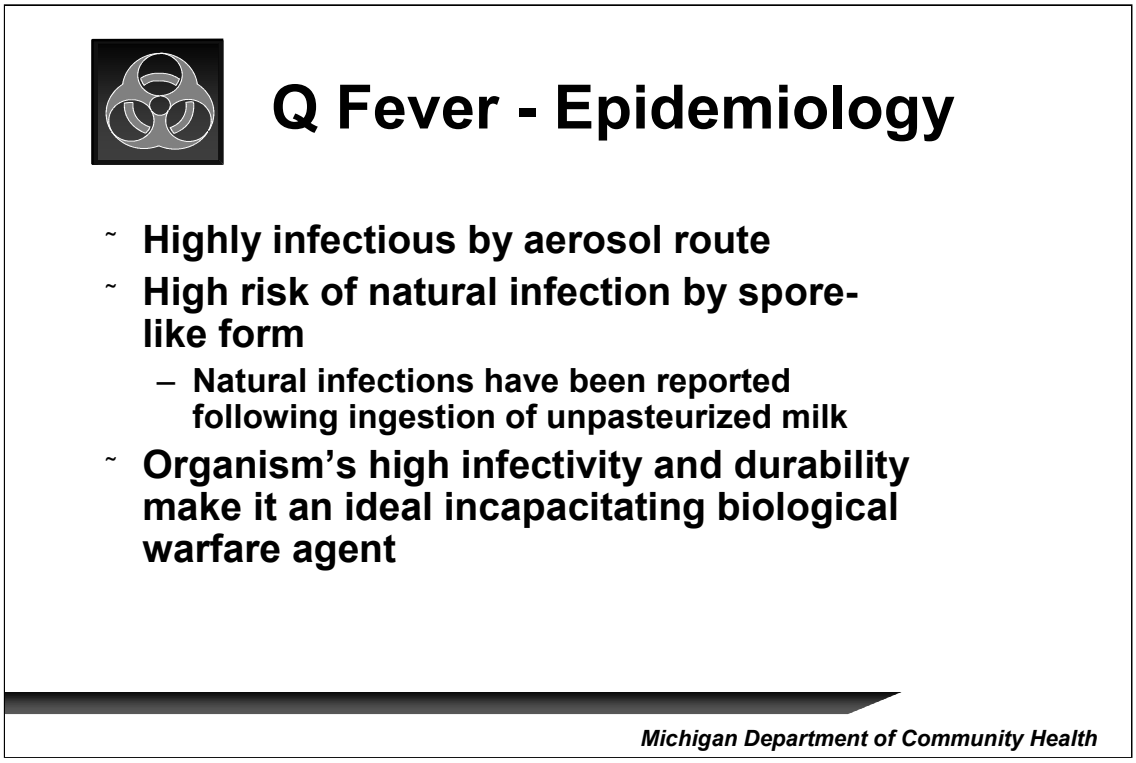
For further information visit our website at www.MDCH.state.mi.us.



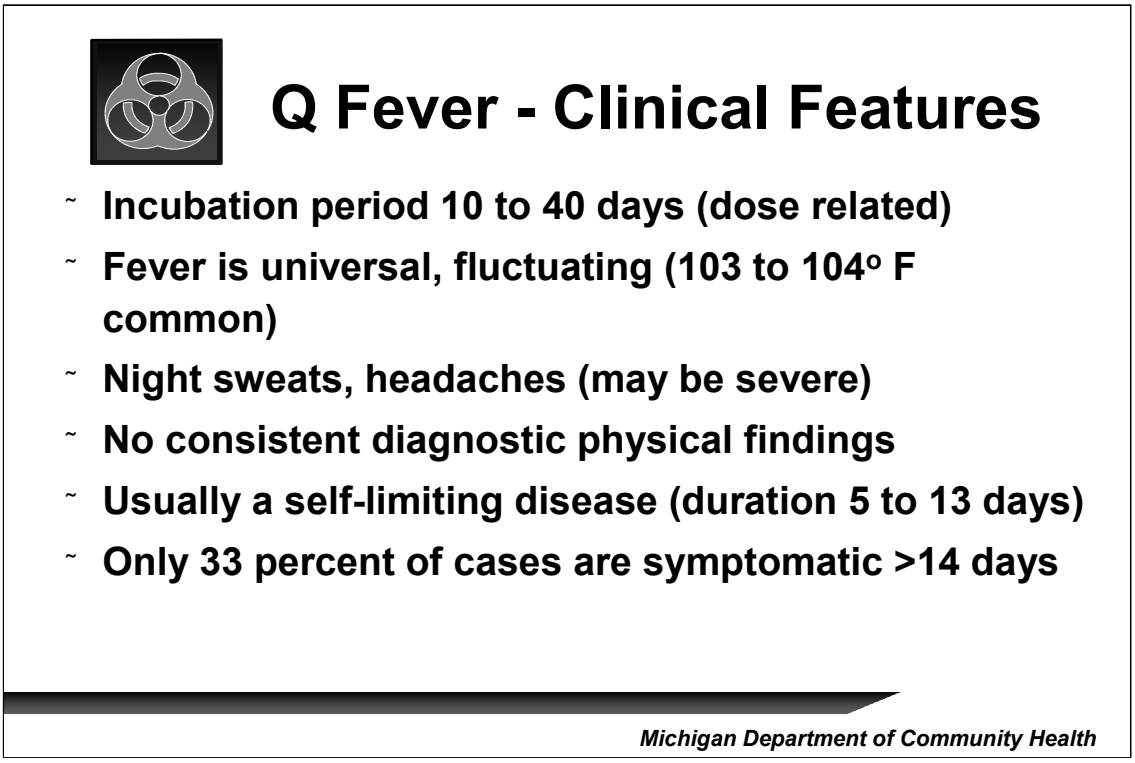
Q fever describes an acute febrile illness caused by the rickettsial-like organism *Coxiella burnetii.* The disease was originally described in 1937 during an outbreak of a previously unknown febrile illness among slaughterhouse workers in Queensland, Australia. The causative agent was isolated by Burnet and Freeman shortly after the description of the disease. This biological agent is considered a zoonotic disease in sheep, cattle, and goats and is distributed worldwide with the exception of New Zealand. In infected animals, the Q fever agent causes only subclinical disease with the exception of spontaneous abortions in pregnant females. However, infectious organisms are excreted in the milk, urine, and feces. Extremely high numbers of organisms are found in the placenta after parturition. Ticks can harbor the organism and contribute to maintenance of the enzootic cycle by trans-ovarial transmission. However tickborne Q fever in humans is rare.

Coxiella burnetii is not considered a true rickettsia although it is classified in the family *Ricketsiaceae.* Although an obligate intracellular parasite of mammalian cells, the organism can survive outside tissue in a spore-like form that is resistant to heat, drying, ultraviolet light, and common disinfectants.

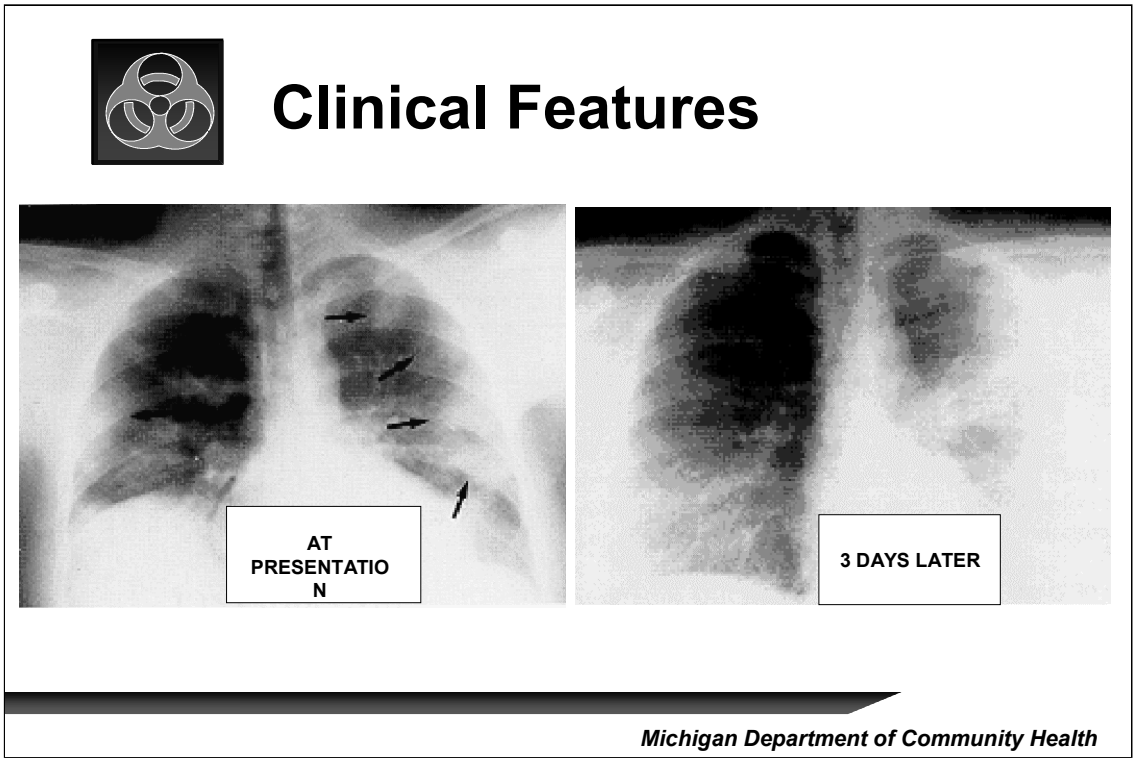
Upon inhalation, *C. burnetii* becomes engulfed within a phagocyte that allows the bacteria to multiply and disseminate to multiple organs and the RES. Initially, the organism causes the host cell to increase its metabolic and functional activity, leading to reduction of the cytoplasm and eventual cell rupture. A single organism is sufficient to cause human disease.



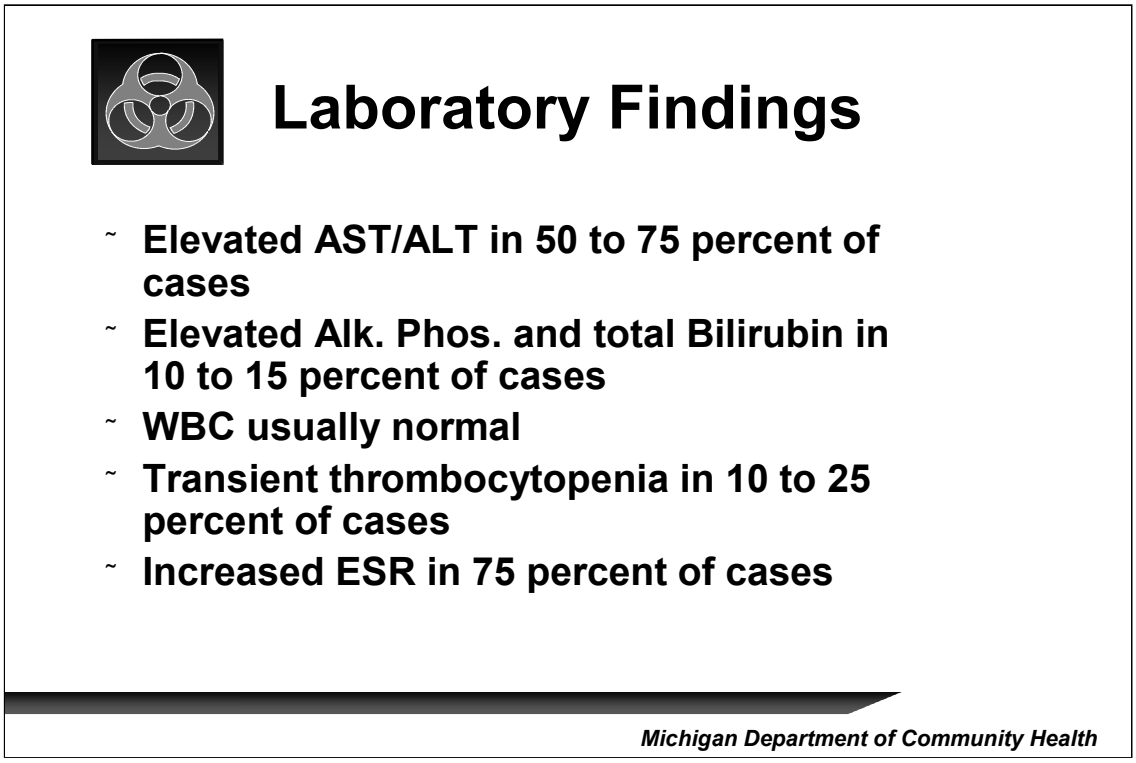
C. burnetii is highly infectious by the aerosol route - a single organism is capable of causing disease in humans. Although Q fever normally causes a self-limiting disease in man, its high infectivity and natural environmental stability have made it an ideal candidate for biological warfare research. Consequently, during the former period of offensive biological warfare development, both the United States and the Soviet Union manufactured Q fever as an aerosolized incapacitating BW agent.



The incubation period for Q fever varies from 10 to 40 days. During this period the organism amplifies in the macrophage / reticuloendothelial system. Natural infections are often asymptomatic or very mild and well over 99 percent of cases will spontaneously recover. In a biological warfare attack, an extremely high number of organisms would be released as an aerosol in the 1 to 5 micron size-range and the number of cases with symptomatic, incapacitating illness would be high.



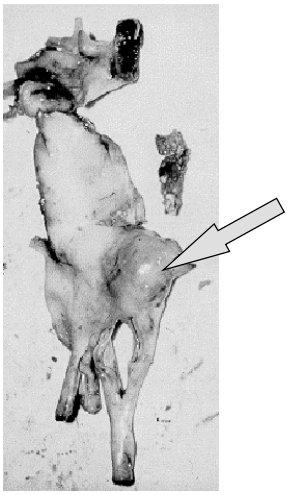
The figure shows serial chest radiographs of a young man who developed Q fever following exposure to an infected animal placenta. Note the multiple rounded opacities in both lung fields (arrows). The opacities coalesce and increase in size over a few days. The basic pathological process is a self-limiting interstitial bronchioloalveolitis with air space consolidation.



Incidental hepatitis can be a feature of Q fever with mild to moderate biochemical abnormalities. Histologically this is characterized by hepatic grannuloma with a characteristic central vacuole and a fibrin ring (doughnut grannuloma). Fulminant hepatic necrosis can occur but this is rare and usually the biochemical and histological changes are transient.

Complications of Q Fever

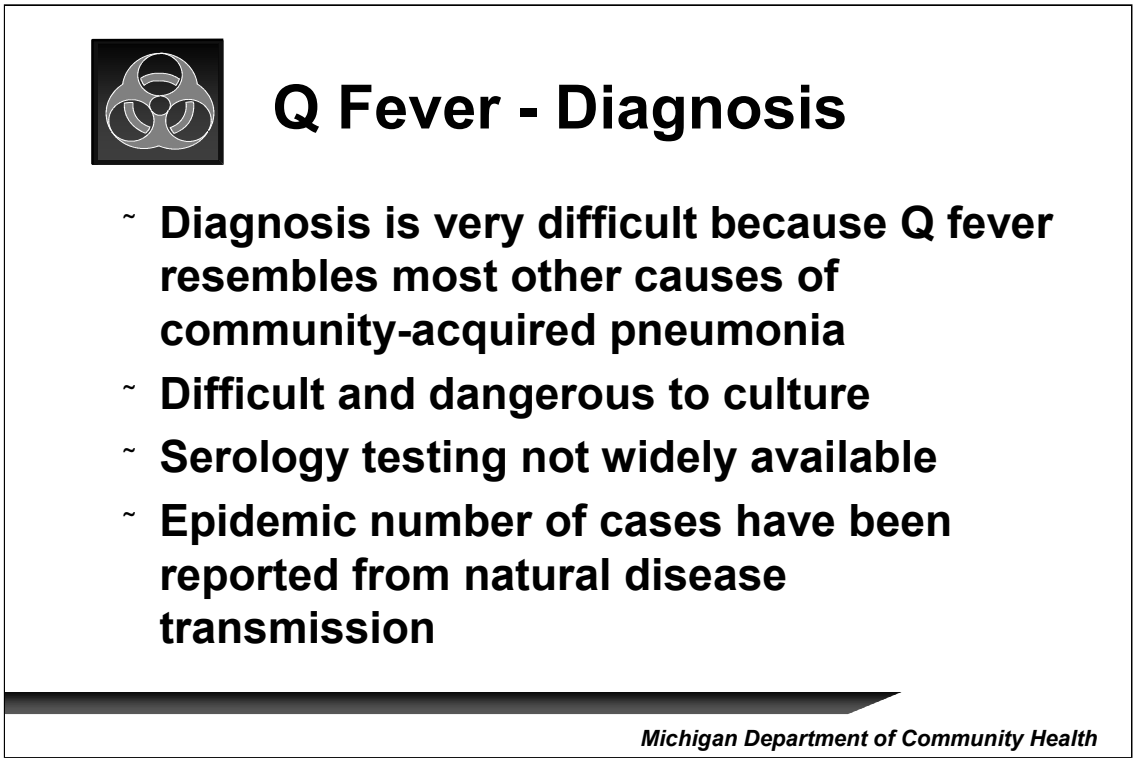
- **Complications are rare, but may include**
  - **Rapidly progressing pneumonia**
  - **Fulminant hepatitis**
  - **Chronic endocarditis**
  - **Osteomyelitis**
  - **Meningitis**



Michigan Department of Community Health

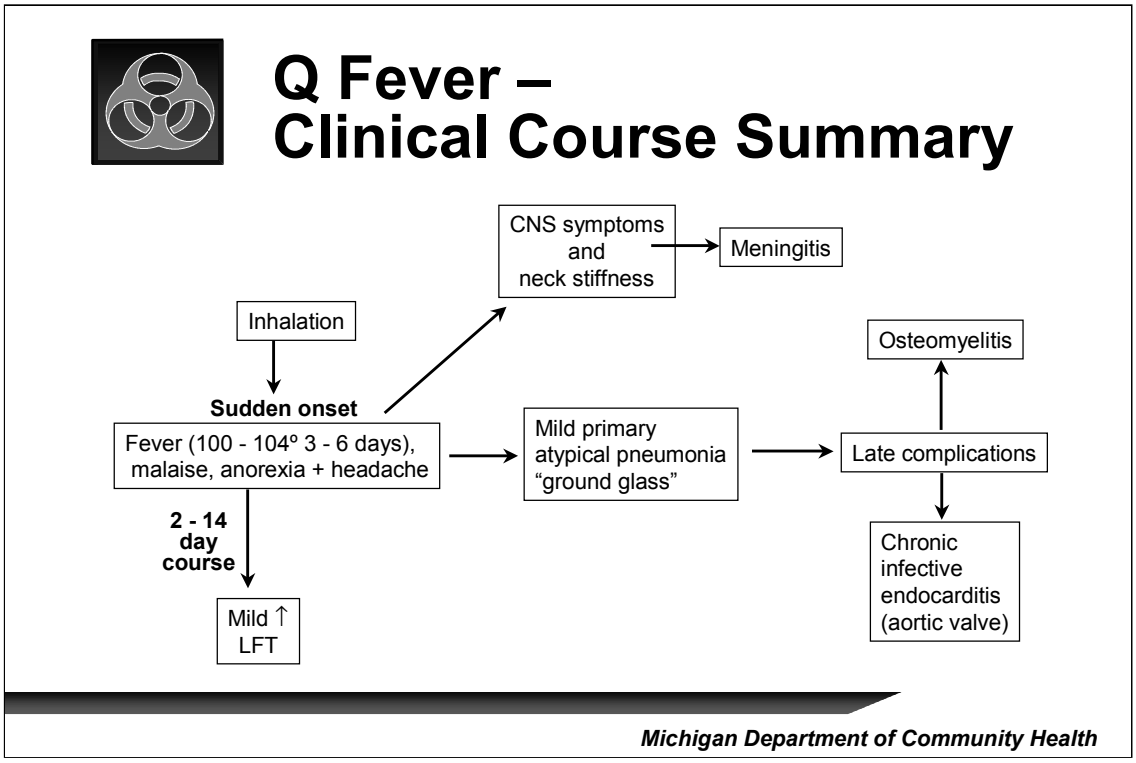
Q fever endocarditis is the most serious complication of *C. burnetii* infection and the clinical picture does not resemble classical endocarditis. Endocarditis may appear years after an acute infection and the most common host factor is underlying heart disease.

NOTE: The photograph demonstrates the mitral valve of a patient with Q fever endocarditis. The nodule on the valve (arrow) was packed tightly with *C. burnetii.*

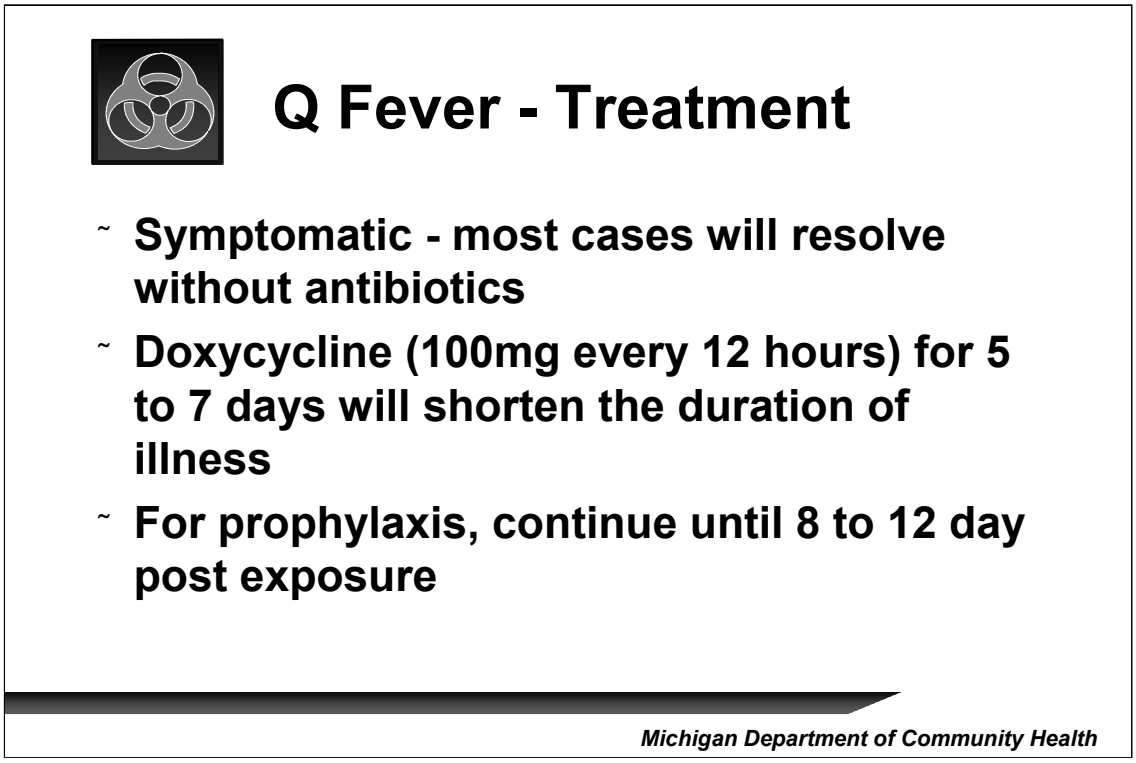


Q fever is very difficult to diagnose because it resembles so many other endemic infectious diseases, including most cases of community acquired pneumonia. The diagnosis should be considered when numerous individuals from the same geographical area present with the same non-specific complaints and findings of pneumonia. Sputum cultures are not usually helpful since the organism is difficult, as well as dangerous, to grow. Serological tests exist, but are not readily available outside of the military.

NOTE: One possible example of the difficulty of diagnosing isolated cases of Q fever, its high infectivity, and the possibility of confusing it with other diseases, comes from two adjacent rural counties in a Midwestern state. The counties reported the first two cases of Q fever in 1984, but a 1988 study indicated that 15 percent of the general population surveyed in the two counties - and 43 percent of those who owned goats - were seropositive for the disease.



Ten to 20 days after inhalation, there is a sudden onset of an influenza-like syndrome with marked anorexia (the etilology of this response is uncertain). The disease runs a 2 to 14 day course marked by 100 - 104º F fever for a few days and an atypical pneumonia in 50 percent of the cases. X-ray may reveal a "ground glass" appearance. One-third of the patients may show liver enzyme elevations. Neck stiffness and CNS signs may also occur. Late complications may include osteomyelitis and chronic infective endocarditis with vegetations occurring primarily on the aortic valve. Blood cultures are negative. The disease is normally self- limiting in non-immunocompromised individuals. Chronic endocarditis with Q fever is normally superimposed on pre-existing cardiac disease.



Treatment for children and adults is symptomatic since **most cases will resolve even without antibiotic therapy**. Giving tetracycline (500 mg every 6 hours) or doxycycline (100 mg twice daily) orally, however, will shorten the duration of the illness. Similar treatment during the incubation period, or as prophylaxis, may delay or prevent the onset of the symptoms depending on when the medication is given.

Q Fever - Prevention of Secondary Infection

- Secondary transmission does not occur
- Universal precautions
- Upgrades to laboratory safety necessary

Michigan Department of Community Health

Person-to-person transmission from patients with Q fever does not occur. Still, universal precautions should be observed. Because a single organism is sufficient to produce infection, safety upgrades must be implemented in areas where potential aerosols could be generated (laboratory centrifuges).

Specimen Collection: Q. Fever

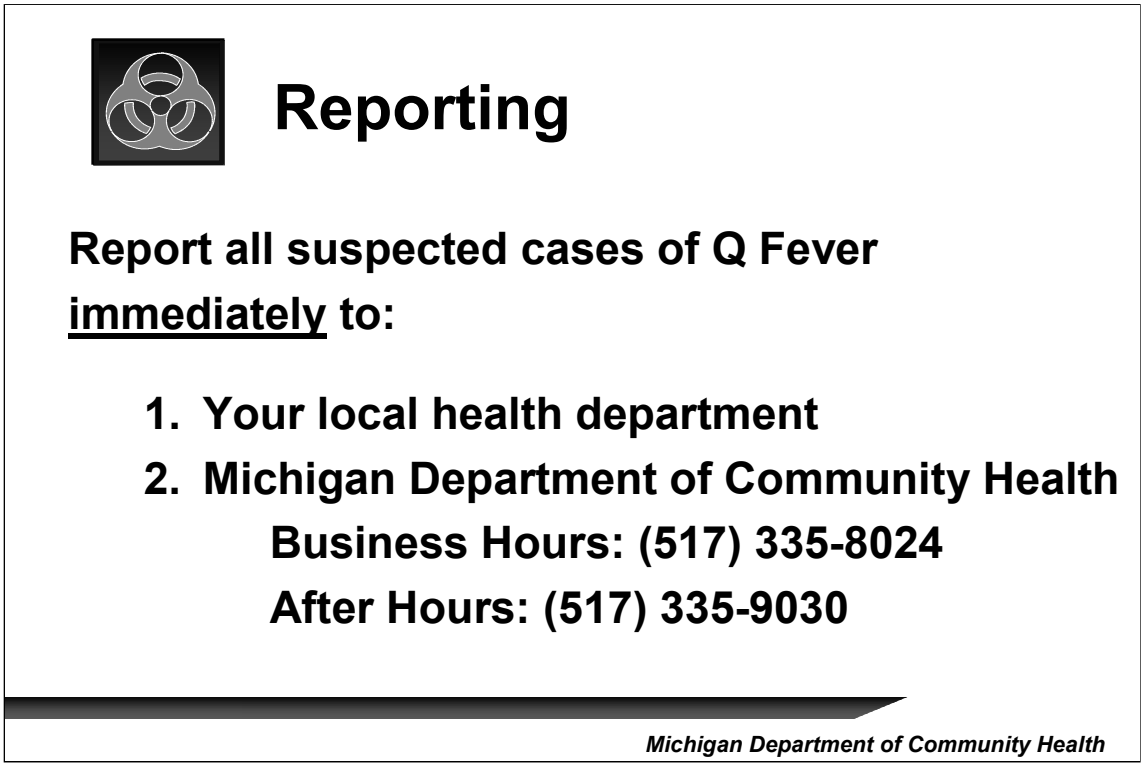
Specimen	Comments
Serum for serology	Collect an acute phase sample and a convalescent phase sample. (10 -12 ml)

Michigan Department of Community Health

The chart above lists the specimens and information related to their collection when testing for infection with Q. Fever.

Specimens should be stored at 4 degrees centigrade.

Specimens collected for Q. Fever must be submitted to the Michigan Department of Community Health Regional Laboratory System or the Michigan Department of Community Health. Contact the Bureau of Laboratories (517-335-8063) for further information on testing prior to submission.

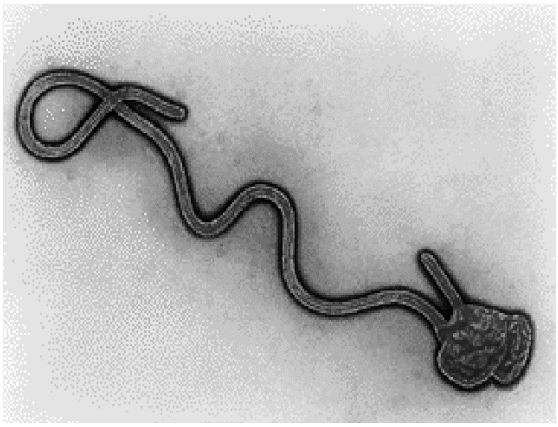


All suspected cases of Q Fever should be reported **immediately** to your local health department and the Michigan Department of Community Health at the phone numbers listed above.

For further information visit our website at www.MDCH.state.mi.us.

Viruses as Biological Agents

- Smallpox
- Viral Hemorrhagic Fevers (VHF)
- Venezuelan Equine Encephalitis (VEE)



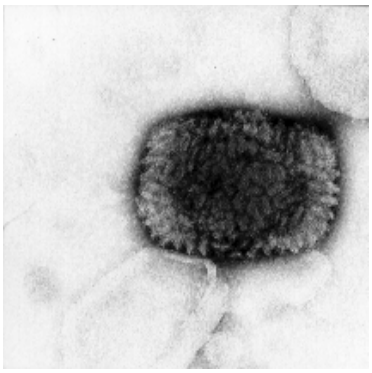
Michigan Department of Community Health

Certain viruses have characteristics that would make them particularly well suited for use as biological agents. These include smallpox and several of the viral hemorrhagic fever (VHF) viruses.

NOTE: Pictured is a color-enhanced micrograph of the virus which causes Ebola hemorrhagic fever.

Smallpox: Overview

- 1980 - Global eradication
- Humans were only known reservoir
- Person-to-person transmission (aerosol/contact)
- Up to 30% mortality in unvaccinated



CDC -Variola major

Michigan Department of Community Health

Smallpox was considered to be eradicated from the world in 1977. In 1980, the World Health Assembly recommended that all countries cease vaccination and that all laboratories destroy their stocks of variola (smallpox) virus or transfer them to one of two World Health Organization reference labs..

The case fatality rate for smallpox is estimated to be 30% with most deaths occurring during the first or second week of illness. Because this virus is relatively stable (not easily destroyed in the environment) and the infectious dose is small, an aerosol release of variola virus would disseminate widely.

Smallpox: Clinical Features

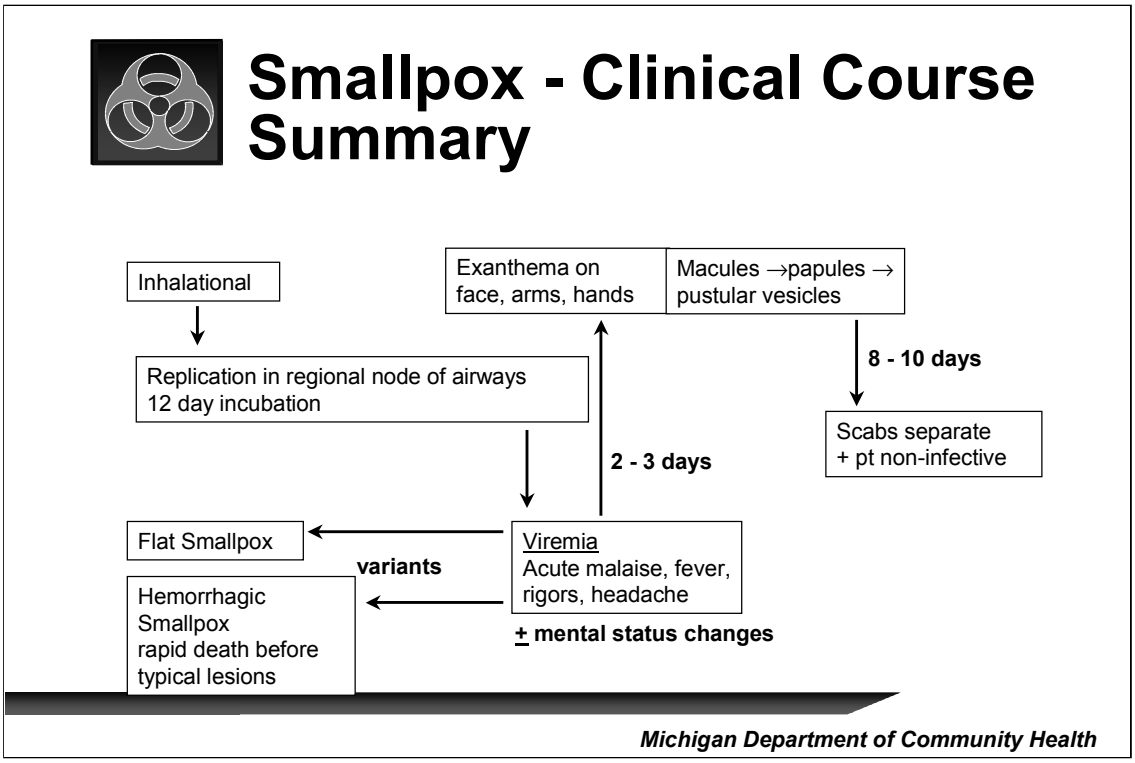
- **Prodrome (incubation 7-17 days)**
  - Acute onset of fever, malaise, headache, backache, vomiting, occasional delirium
  - Transient erythematous rash
- **Exanthem**
  - Begins face, hands, forearms
  - Spread to lower extremities then trunk over ~ 7 days
  - Synchronous progression: macules --> vesicles --> pustules --> scabs
  - Lesions on palms /soles

USAMRICD

Michigan Department of Community Health

At the end of the incubation period the patient typically experiences high fever, malaise and prostration with headache and backache. Severe abdominal pain and delirium are sometimes present. A maculopapular rash then appears on the mucosa of the mouth and pharynx, face and forearms and spreads to the trunk and legs. Within 1 to 2 days, the rash becomes vesicular and, later, pustular. The pustules are characteristically round, tense, and deeply embedded in the dermis; crusts begin to form on about the eighth or ninth day.

[Picture of prominent lesions on face at later stage of illness]



Airway exposure to the virus is followed by viral replication in the regional lymph nodes of the airways. Viremia occurs 12 days later with the onset of an influenza-like syndrome.

There are 2 sequences of viremia. The first 4 days post infection is asymptomatic, resulting in spread to the spleen, liver etc. The second round of viremia on about the eighth day and localizes virus in microcirculation below skin and in pharynx again. The rash presents 2-4 days later.

The virus disseminates to the spleen, liver and lung, and an initial mild erythematous rash is followed 2 to 3 days later by exanthema on the face, arms, and hands. Over a period of 8 to 10 days, the macules become papules and typical pustular vesicules.

Clinical variants of typical variola virus infection include flat smallpox and hemorrhagic smallpox in immunocompromized patients. Rapid death often occurs before typical lesions have time to develop.

Smallpox: Complications

- **Encephalitis (1 in 2,000 cases)**
- **Keratitis, corneal ulceration**
  - Blindness in 1% of cases
- **Infection in pregnancy**
  - High perinatal mortality
  - Congenital infection

Michigan Department of Community Health

Except for the lesions on the skin and mucous membranes and reticulum cell hyperplasia, other organs are seldom involved. Secondary bacterial infection is not common, and death most likely results from the toxemia associated with circulating immune complexes and soluble variola antigens.

Smallpox vs. Chickenpox

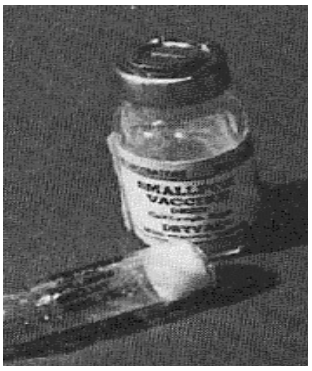
	Variola	Varicella
Incubation	7-17 days	14-21 days
Prodrome	2- 4 days	minimal/none
Progression	synchronous	asynchronous
Scab formation	10-14 d p rash	4-7 d p rash
Scab separation	14-28 d p rash	<14 d p rash

Michigan Department of Community Health

If today's physician were to encounter a patient with early symptoms of smallpox infection, the most likely differential diagnosis would be chickenpox. The most identifiable difference between smallpox and chickenpox is the progression of the rash. It is also important to note that chickenpox would be much less likely to present in an adult patient.

Smallpox Vaccination

- **Made from live Vaccinia virus**
  - 15.4 million doses in US Stores
- **Intradermal inoculation with bifurcated needle (scarification)**
  - Pustular lesion or induration surrounding central lesion (scab or ulcer) 6-8 days post-vaccination
  - Low grade fever, axillary lymphadenopathy
  - Scar (permanent) demonstrates successful vaccination
  - Immunity not life-long



WHO

Michigan Department of Community Health

Current stocks of smallpox vaccine were produce from another live virus (vaccinia virus) that promotes an immune response to smallpox virus without risk of infection. The unique method of vaccine delivery involves utilization of a bifurcated needle for scarification and inoculation. A scar after vaccine administration has been used as evidence of successful immunization.

This vaccine does NOT provide life-long immunity.

Smallpox: Vaccination Complications

- **Most common**
  - Inadvertent inoculation (skin, eye)
- **Less Common**
  - Generalized vaccinia
  - Post-vaccination encephalitis (2.8/million)
  - Fatal vaccinia
  - Eczema vaccinatum (4.5/million)
  - Vaccinia necrosum (0.7/million)
- **Primary vaccination - 1 death/million**
- **Revaccination - 0.2 deaths/million**

Michigan Department of Community Health

The smallpox vaccination is considered relatively safe but not completely without risks. The most common complication of vaccination is self-inoculation of another area of the body with resultant pustule. Less common is the presentation of generalized infection which can occur in persons with underlying immunosuppression or skin disorders such as eczema

It is important to note that the healing pustule from a vaccinated individual has live vaccinia virus which can cause infection (local or generalized) in unvaccinated individuals until scabbed over/healed

[Pictures:Self inoculation of eye after vaccination; Vaccinia necrosum]

Smallpox: Vaccinia Immune Globulin (VIG)

- **Treatment of adverse reactions (AR)**
  - Approximately 25AR's/100,000 vaccinations
  - AR rate may be increased due to higher immunocompromised population
- **Post-exposure prophylaxis**
  - Pregnant patients (VIG + Vaccinia vaccine)
  - Eczema (VIG + Vaccina vaccine)
  - Immunocompromised patients, No consensus (VIG alone vs. VIG + Vaccinia vaccine?)
- **Current supplies very limited**

Michigan Department of Community Health

Earmarked primarily for use in the treatment of individuals with adverse vaccine reactions current stores of VIG will be available from the CDC under an Investigational New Drug label (IND). It is estimated that today, complications due to vaccination adverse reactions may be higher than previously seen due to higher immunocompromised population.

**These treatments are not recommended for women and children therefore their use in a specific clinical setting must be decided upon the basis of their risk versus the benefit to the patient.

Smallpox: Medical Management

- **Strict airborne precautions and contact isolation of patient**
  - Patient infectious until all scabs have separated
- **Notify public health authorities <u>immediately</u> for suspected case**
- **Identification of contacts within 17 days of the onset of case's symptoms**

Michigan Department of Community Health

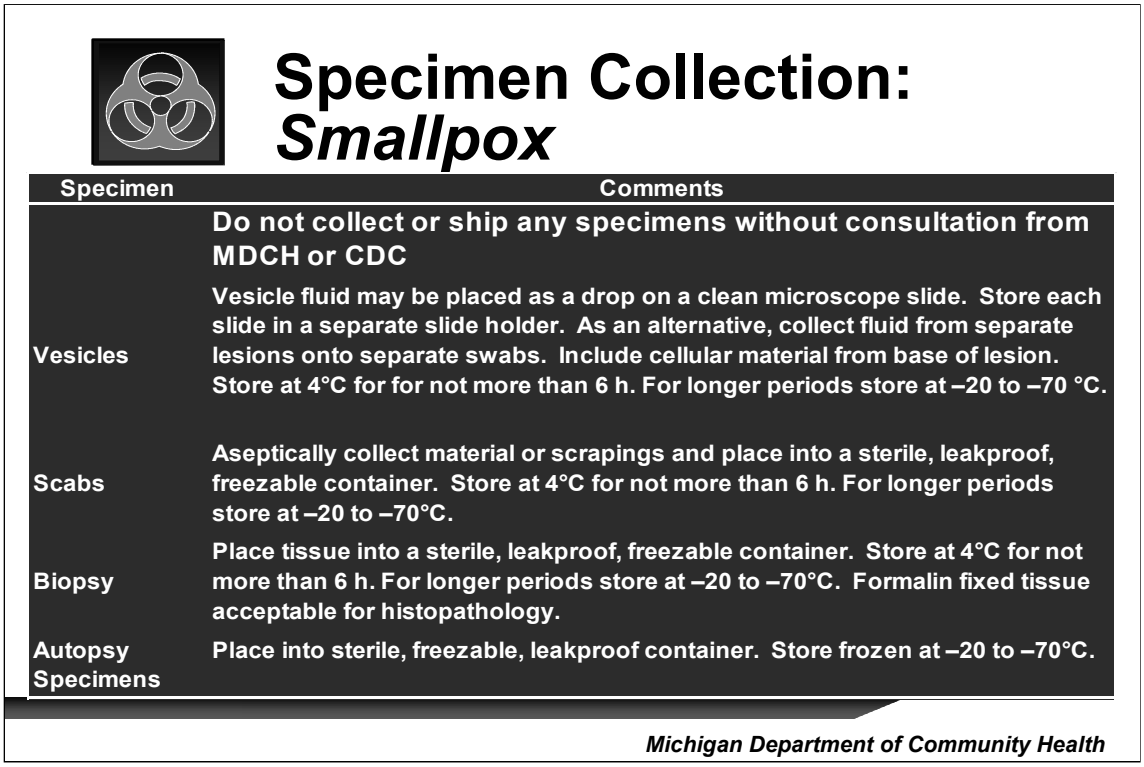
Smallpox patients are highly contagious by respiratory as well as contact routes. Airborne precautions should include the use of a fit tested N95 mask. Contact to all suspected cases must be limited as much as possible and emphasis should be placed on the isolation of patients and contact tracing to limit spread of disease.

Smallpox: Management of Contacts

- **Immediate vaccination (or boosting) of ALL potential contacts including health care workers**
  - Vaccination within 4 days of exposure may prevent or lessen disease burden
  - 17 days observation for fever or rash
- **Passive immunization (VIG)**
  - Potential use for contacts at high risk for vaccine complications (pregnancy, dermatoses, immunosuppression)

Michigan Department of Community Health

When contacts are identified, they should initially be evaluated for symptoms. Contacts without clinical signs of disease should receive vaccination (VIG may potentially be used for contacts having contraindications to vaccination). To control the spread of disease, all contacts should be observed for fever or rash illness and consideration should be given to limiting contact travel until the end of the incubation period.



The chart above lists the specimens and information related to their collection when testing for infection with Smallpox.

Do not collect or ship any specimens without prior consultation from the Michigan Department of Community Health, Bureau of Laboratories 517-335-8063.

Reporting

Report all suspected cases of Smallpox <u>immediately</u> to:

1. **Your local health department**
2. **Michigan Department of Community Health**
   Business Hours: (517) 335-8024
   After Hours: (517) 335-9030

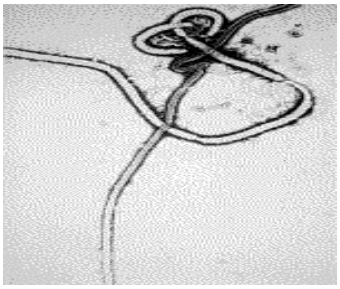
Michigan Department of Community Health

All suspected cases of Smallpox should be reported **<u>immediately</u>** to your local health department and the Michigan Department of Community Health at the phone numbers listed above.

For further information visit our website at www.MDCH.state.mi.us.

Viral Hemorrhagic Fevers (VHF): Overview

- **Caused by several different viruses families**
  - Filoviruses (Ebola, Marburg)
  - Arenaviruses (Lassa, Junin, Machupo, Sabia, Guanarito)
  - Bunyaviruses
  - Flaviviruses
- **Natural vectors - virus dependent**
  - rodents, mosquitoes, ticks
- **<u>No</u> natural occurrence in U.S.**



CDC

Michigan Department of Community Health

Syndrome caused by several different virus families. Ones of highest concern for biological terrorism are from the Filo and Arena virus groups. There are different natural vectors for these viruses. While vectors may be present in the United States as yet, these viruses do not occur naturally in US.

[Picture is an electron micrograph of the Ebola virus]

VHF: Clinical Information

- **Usual patient history**
  - Foreign travel to endemic or epidemic area
  - Rural environments
  - Nosocomial exposure
  - Contact with arthropod or rodent reservoir
  - Domestic animal blood exposure
- **Incubation**
  - Typical 5 to 10 days
  - Range 2 to 16 days

Michigan Department of Community Health

Because this syndrome does not naturally occur within the US, it is important to obtain a complete history from a patient with a potentially naturally contracted case of VHF. This history should include the identified range of incubation periods (2 to 16 days). *Patient with disease due to bioterrorist event may have none of these identified risk factors.*

VHF: Clinical Presentation

- **Symptoms**
  - Fever, headache, malaise, dizziness
  - Myalgias
  - Nausea/vomiting
- **Initial signs**
  - Flushing, conjunctival injection
  - Periorbital edema
  - Positive tourniquet test
  - Hypotension

Michigan Department of Community Health

Generally all cases of VHF present in a similar fashion. Beginning with non-specific early symptoms of fever, malaise, headache and myalgias, they progress to include symptoms of conjuntival injection, periorbital edema and hypotension.

VHF: Clinical Presentation

- **Other signs/symptoms**
  - Prostration
  - Pharyngeal, chest, or abdominal pain
  - Mucous membrane bleeding, ecchymosis
  - Shock
- **Usually improving or moribund within a week (exceptions: HFRS, arenaviruses)**
- **Bleeding, CNS involvement, marked SGOT elevation indicate poor prognosis**
- **Mortality: agent dependent (10 to 90%)**

Michigan Department of Community Health

The illness continues to progress in patients to include severe prostration, bleeding, and shock. Usually patients will show signs of improvement or worsening within a week of onset (with the exception of patients with hemorrhagic fever with renal syndrome (HFRS) or those with arenavirus infections). Signs of a poor prognosis include bleeding, CNS involvement and SGOT (AST) level elevation.

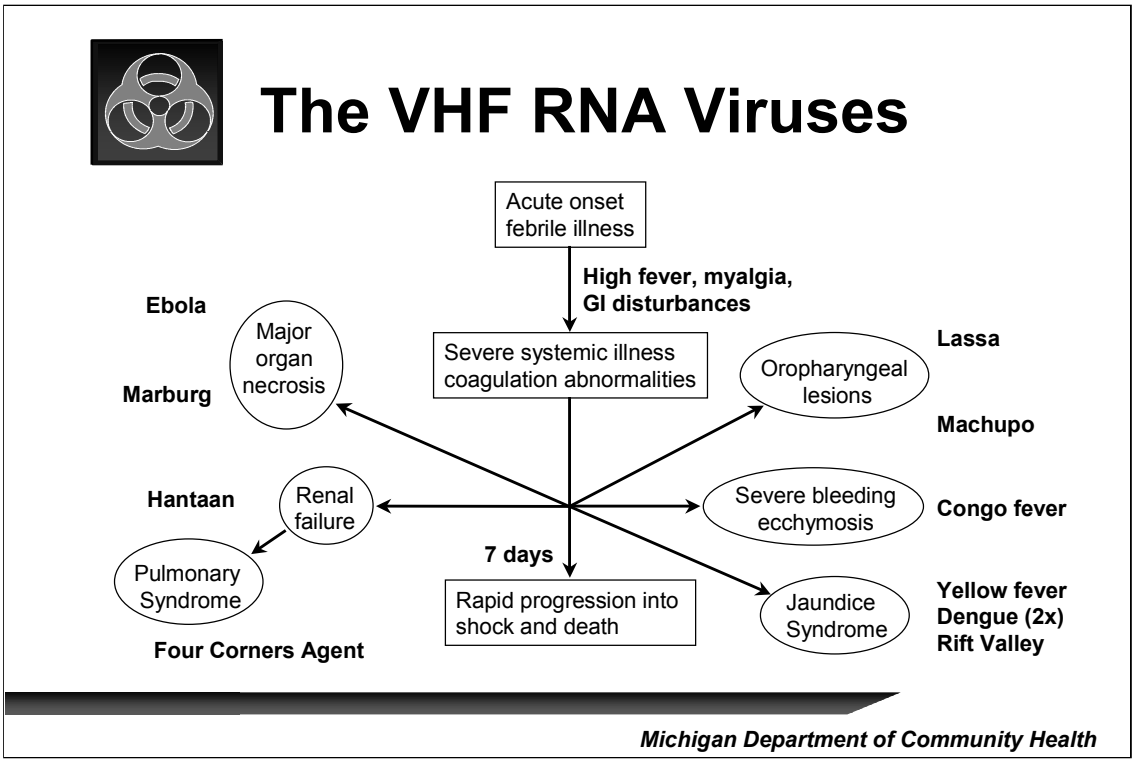
VHF mortality is very dependent on causative viral agent ranging from 10% for Lassa virus to 90% for the Zaire strain of the Ebola virus.

VHF: Differential Diagnosis

- **Bacterial**
  - Typhoid fever, meningococcemia, rickettsioses, leptospirosis
- **Protozoa**
  - Falciparum malaria
- **Other**
  - Vasculitis, TTP, Hemolytic Uremic Syndrome (HUS), heat stroke

Michigan Department of Community Health

Many diseases of differing etiologies can mimic VHF including: Leptosporosis, Meningococcemia, Rocky Mountain Spotted Fever, Malaria, and other diseases of non-infectious etiologies such as TTP and vasculitis



The Viral Hemmorhagic Fevers (VHF) are a group of disorders caused by five different families of virus. Members of the *Flaviviridae* include Dengue and Yellow Fever which are transmitted by mosquitoes. The *Arenavirdae* are carried by rodents in South America and Africa and cause the diseases named Lassa and Machupo Hemmorhagic Fever. The *Bunyaviridae* encompass Rift Valley Fever and Congo-Crimean Hemorrhagic Fever, also naturally transmitted by insects. The VHF caused by the *Hantavirus* family include hemorrhagic fever with renal syndrome and the lethal Sin Nombre viral agent which emerged unexpectedly in the four corners region of the Southwest United States in 1994. The most famous of the VHF viruses are the *Filoviridae*, which cause the deadly diseases of Ebola and Marburg Virus Disease.

Each of these viruses cause its own unique viral hemorrhagic fever syndrome. Congo-Crimean Hemorrhagic Fever is characterized by massive bleeding abnormalities and extensive ecchymoses which dominates the clinical picture. The HFRS hantavirus infection is characterized by extensive renal involvement and a long incubation period. Rift Valley Fever and Yellow Fever may feature extensive hepatic involvement. The natural reservoirs for the *Filoviridae* (Ebola and Marburg Virus Disease), are unknown at this time.

In spite of the diverse viral taxonomy and variable forms of clinical disease, the VHF share a common generalized clinical presentation.

NOTE: Animal model studies suggest that the Ebola filovirus can be transmitted by aerosol, and the virus has many characteristics that would make it a viable biological warfare agent.

VHF: Treatment

- Supportive care
- Cautious sedation and analgesia
- Correct coagulopathies as needed
- No antiplatelet drugs or IM injections
- Ribavirin effective for:
  - Arenaviruses
  - Bunyaviridae (CCHF, Hantaan, RVF)

Michigan Department of Community Health

There is no standard treatment for VHF. Currently, patients receive supportive therapy. This consists of balancing the patient's fluids and electrolytes, maintaining their oxygen status and blood pressure, and treating them for any complicating infections.

During a large outbreak of Ebola HF in Kikwit, Democratic Republic of the Congo, in 1995, eight patients were given blood of individuals who had recovered from previous Ebola infections. Seven of the eight patient survived. However, because the study size was small, and because the characteristics of the participants predisposed them towards recovery, the efficacy of the treatment remains unknown.

For Marburg infection, treatment also has included transfusion of fresh-frozen plasma and other preparations to replace the blood proteins important in clotting. One controversial treatment involves the use of heparin (which blocks clotting) to prevent the consumption of clotting factors. Some researchers believe the consumption of clotting factors is part of the disease process.

Ribavirin, an antiviral drug, has been used with success in Lassa fever patients. It has been shown to be most effective when given early in the course of other VHF illnesses. Patients should also receive supportive care consisting of maintenance of appropriate fluid and electrolyte balance, oxygenation and blood pressure, as well as treatment of any other complicating infections.

**These treatments are not generally recommended for women and children. Their use in a specific clinical setting must be decided upon the basis of their risk versus the benefit to the patient.

VHF: Patient Isolation

- **Single room w/ adjoining anteroom (if available)**
  - Handwashing facility with decontamination solution
- **Negative air pressure**
- **Strict barrier precautions including protective eyewear/faceshield**
- **Disposable equipment /sharps in rigid containers with disinfectant then autoclave or incinerate**
- **All body fluids disinfected**

Michigan Department of Community Health

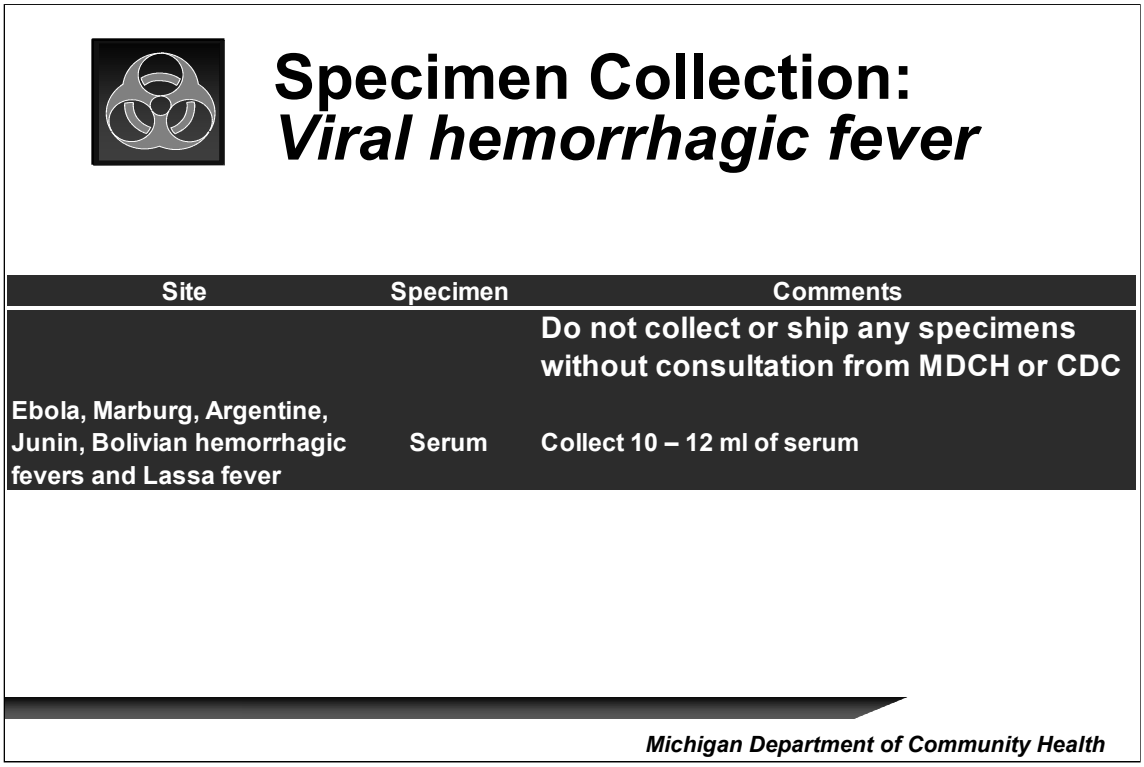
Strict patient isolation is necessary for VHF caused by Filo and Arenaviruses. It is not required for identified cases of Yellow Fever, Rift Valley Fever, or Dengue Fever (other VHFs). The most important patient isolation measures include barrier precautions for bodily fluids and respiratory droplet precautions. All contaminated medical supplies must be properly disposed of to prevent transmission of disease to health care workers and other patients.

VHF: Contact Management

- **Casual contacts - No known risk**
- **Close contacts**
  - Household, physical, nursing, handle lab specimens
  - Record temp b.i.d. for 3 weeks post-exposure
  - Consider prophylaxis (Ribavirin) if temp > 101°F or other systemic symptoms within 3 weeks
- **High-Risk contacts**
  - Mucous membrane, penetrating injury with exposure to body fluids or tissue
  - Consider post-exposure prophylaxis

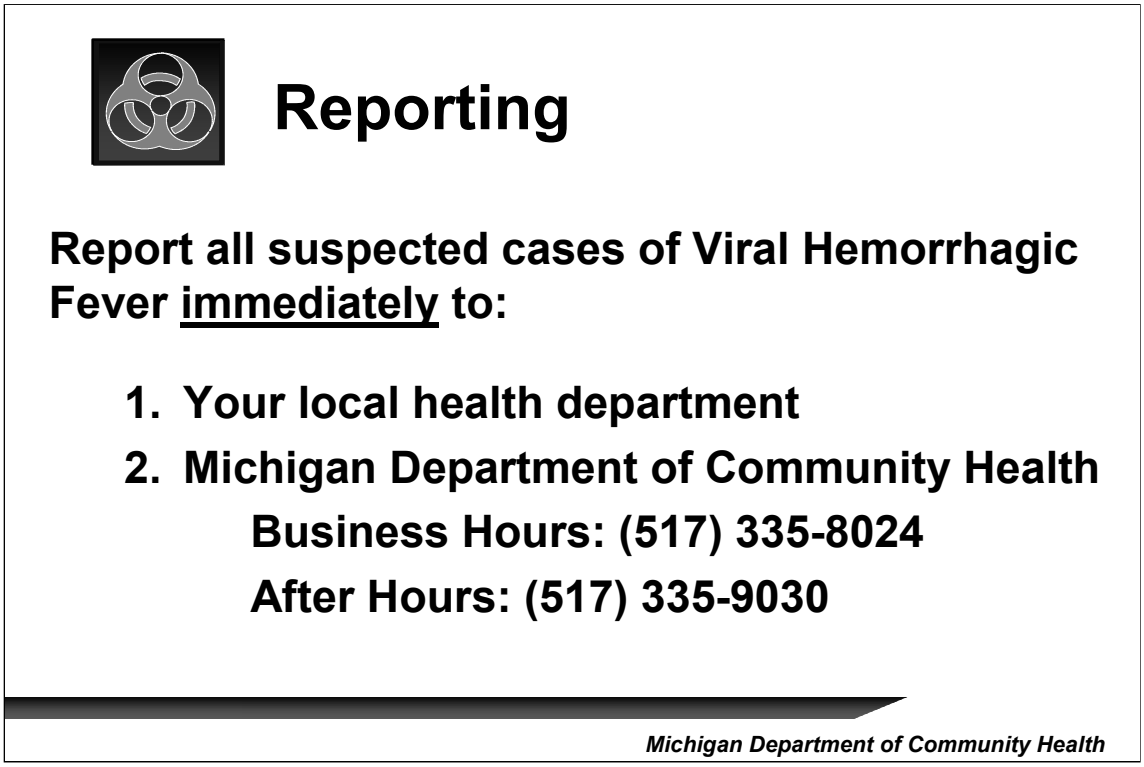
Michigan Department of Community Health

Casual contacts of VHF patients are not considered to be at increased risk of infection. All close contacts should be monitored and prophylaxsis with Riboavirin should be considered if they become febrile within 3 weeks of exposure. Immediate post-exposure prophylaxis should be considered for high-risk contacts. However, current research has not identified a clearly appropriate dose, route of administration (PO/IV) or duration for post-exposure Ribavirin treatment.



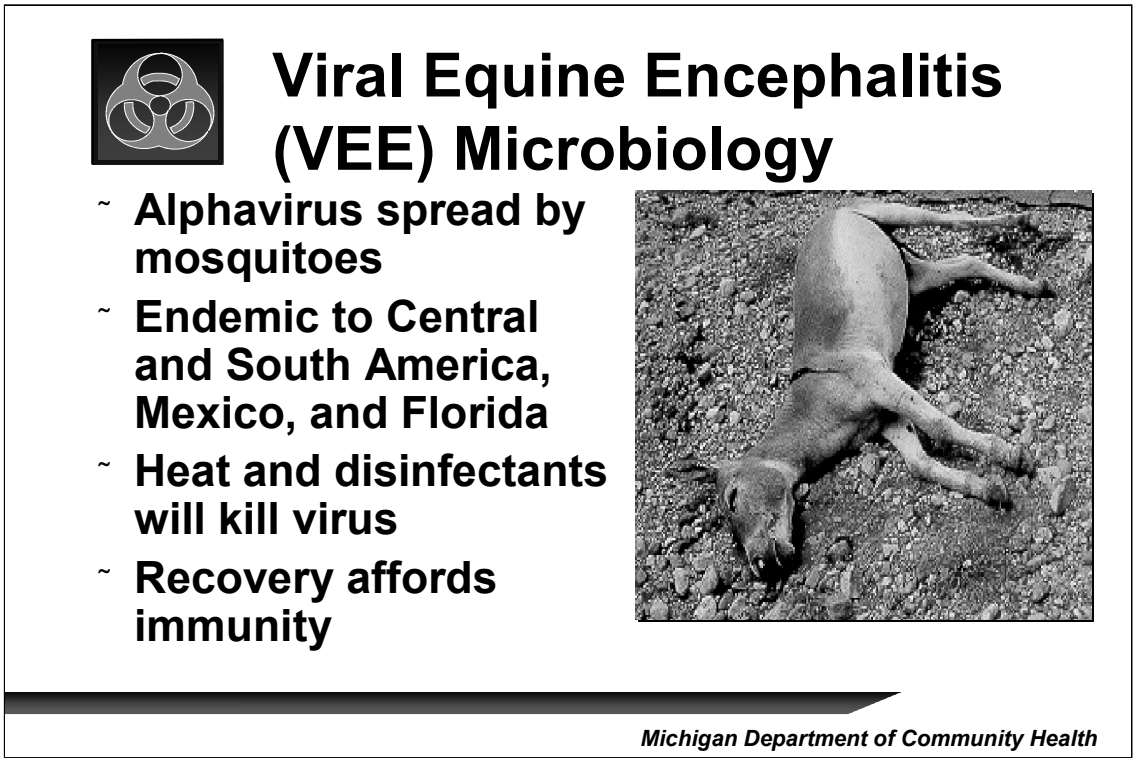
The chart above lists the specimens and information related to their collection when testing for infection with Viral hemorrhagic fever.

Do not collect or ship any specimens without prior consultation from the Michigan Department of Community Health, Bureau of Laboratories at 517-335-8063.

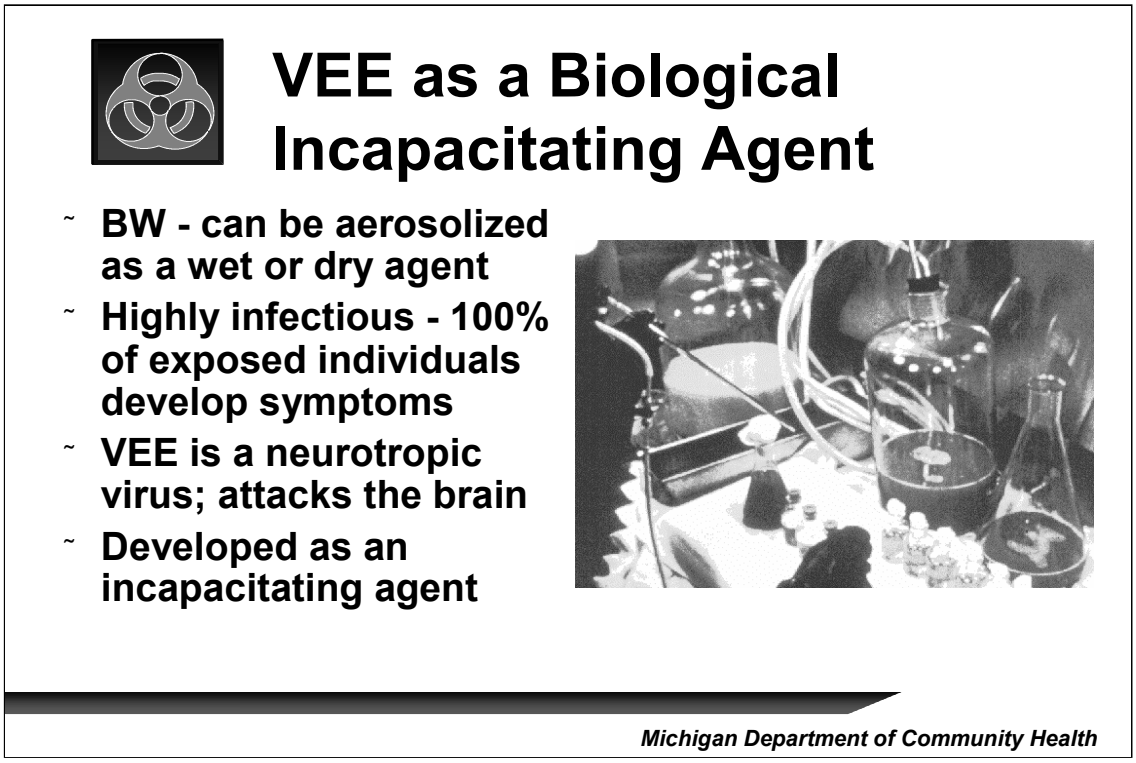


All suspected cases of Viral Hemorrhagic Fever should be reported **immediately** to your local health department and the Michigan Department of Community Health at the phone numbers listed above.

For further information visit our website at www.MDCH.state.mi.us.



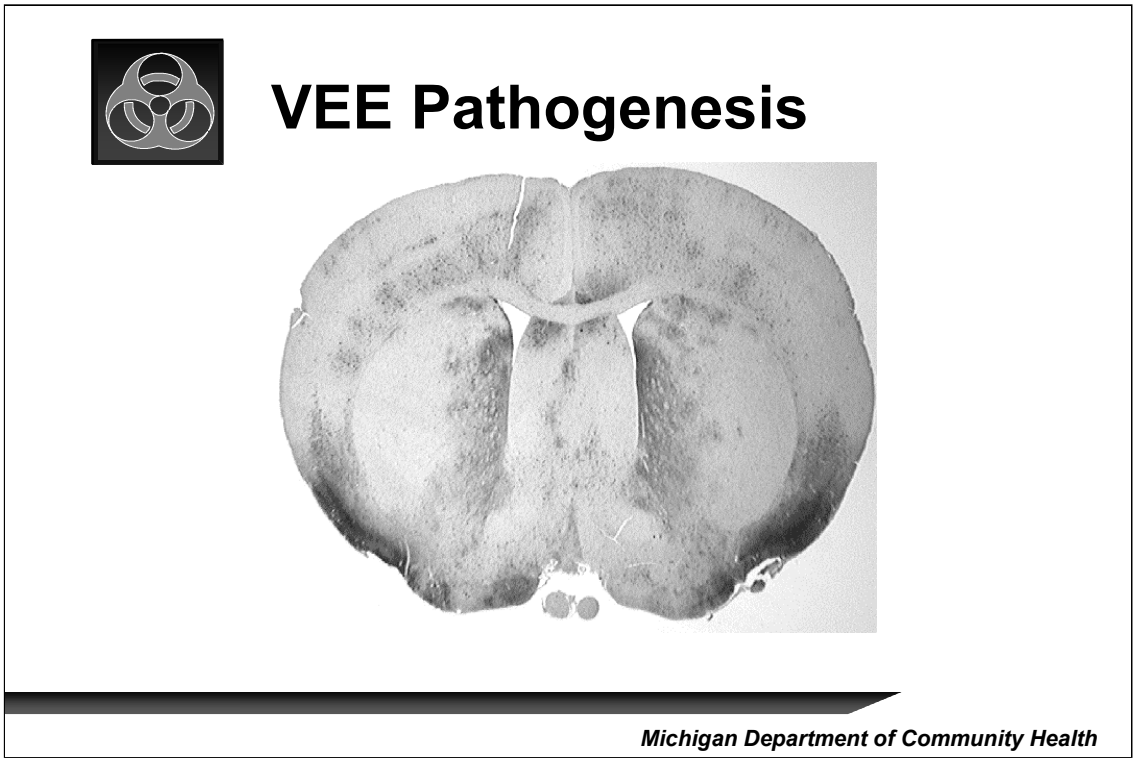
Viral Equine Encephalitis (VEE) virus is a mosquito-borne alphavirus that is endemic in certain parts of the world (Central and South America, Mexico, and Florida) infecting horses, mules, and donkeys. If this agent was intentionally released as an aerosol, disease might occur simultaneously in both horses and humans, but this pattern might not be commonly recognized in some parts of the U.S. Heat and disinfectants easily kill the virus.



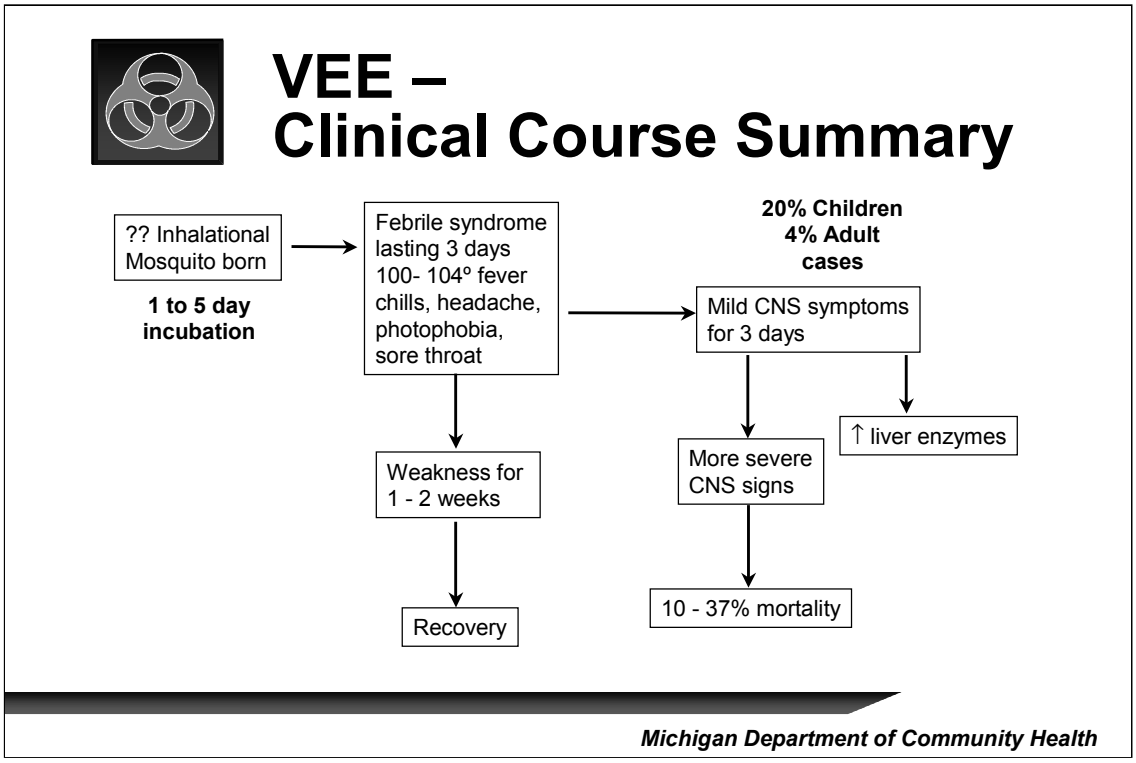
VEE is highly infectious, with nearly 100 percent of exposed individuals developing symptoms. However, only about 1 percent will die. Recovery from an infection results in excellent short-term and long-term immunity.

The VEE virus can be cultured in embryonated chicken eggs, the infected embryos removed and homogenized into a red-colored wet slurry. Dry powder preparations were also developed for offensive BW use

NOTE: VEE mortality rate of 1 percent is observed in natural infection by vector mosquitoes. However, terrorist use of VEE as an aerosol would be likely to have a considerably higher mortality, considering the virus is trophic for the olfactory nerves and could gain access to the CNS via this route. Children may exhibit more severe CNS signs. The exact reason for this age difference in morbidity/mortality is not clear, but alpha viruses have recently been shown to endure apoptosis (programmed cell death) in young neurons in tissue culture.

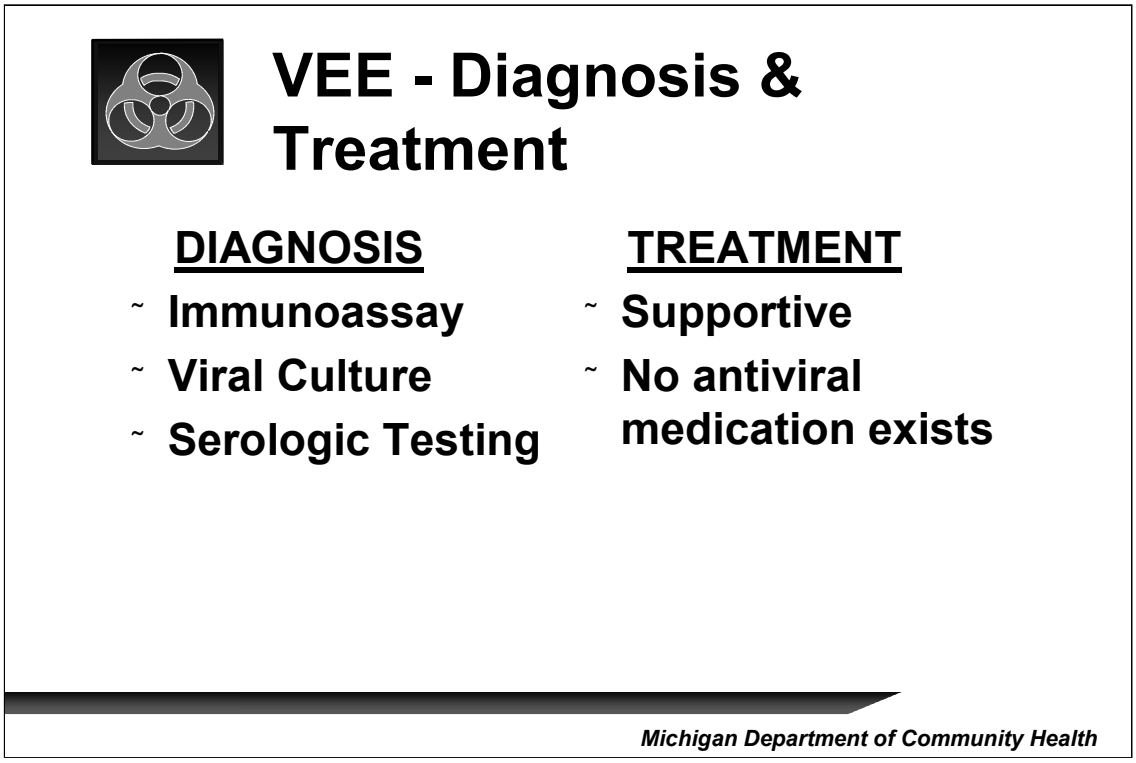


The VEE virus is extremely neurotropic, the virus has the necessary proteins to strongly bind to nerve cell membranes and be taken inside the cell where it replicates into new viral particles. The slide above demonstrates a section of brain tissue infected with the VEE virus. The proteins of the virus have been stained brown by immunohistochemistry using antibodies specific for the virus. The widespread encephalitis apparent in this tissue section is the cause of the fatalities associated with this disease.



After exposure to the virus, symptoms begin to develop in 1 to 5 days. These consist of spiking fevers to 104º F, rigors, severe headache, photophobia, myalgias, nausea, vomiting, and diarrhea. These severe symptoms tend to last up to 3 days, followed by a prolonged period of weakness and lethargy. Most patients recover in 1 to 2 weeks.

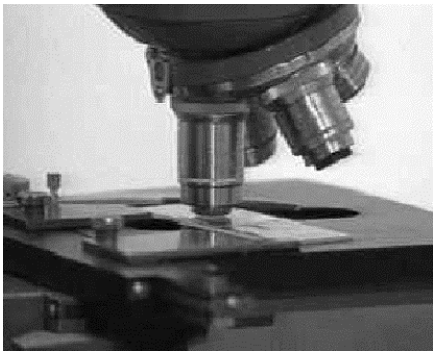
CNS symptoms secondary to meningitis and encephalitis are characteristics of VEE, but only a small percentage of victims (20 percent of children, 4 percent of adults) will actually develop these symptoms in the naturally acquired disease. In a BW aerosol, based on primate studies, the virus would tend to infect the olfactory bulb through the cribriform plate and a greater percentage of CNS involvement might occur. If patients develop CNS disease (meningitis, seizures, change in mental status, or coma), especially in children, the overall mortality rate becomes much higher (up to 20 percent). Permanent neurologic sequela have been reported.



Immunoassay, viral culture, or serological testing may confirm the diagnosis. Treatment is primarily supportive since no antiviral medication exists. Most patients should be treated with pain medications, while those with encephalitis may require anticonvulsant therapy.

VEE - Prevention of Secondary Transmission

- Direct person-to-person spread does not occur without an insect vector
- Universal precautions
- Kill insects to remove natural vector in environment



Michigan Department of Community Health

Secondary spread by person-to-person contact does not occur; however, universal precautions still should be practiced.

Regions where suitable mosquito vector species are present should intensify insect spraying programs following a biological attack to prevent the establishment of endemic disease.

Specimen Collection: Viral Equine Encephalitis

Specimen	Comments
Serum for serology	Collect an acute phase sample as soon as possible after onset of disease. Collect convalescent phase sample 10-14 days after the acute sample. (10 -12 ml, 2.5ml minimum)

Michigan Department of Community Health

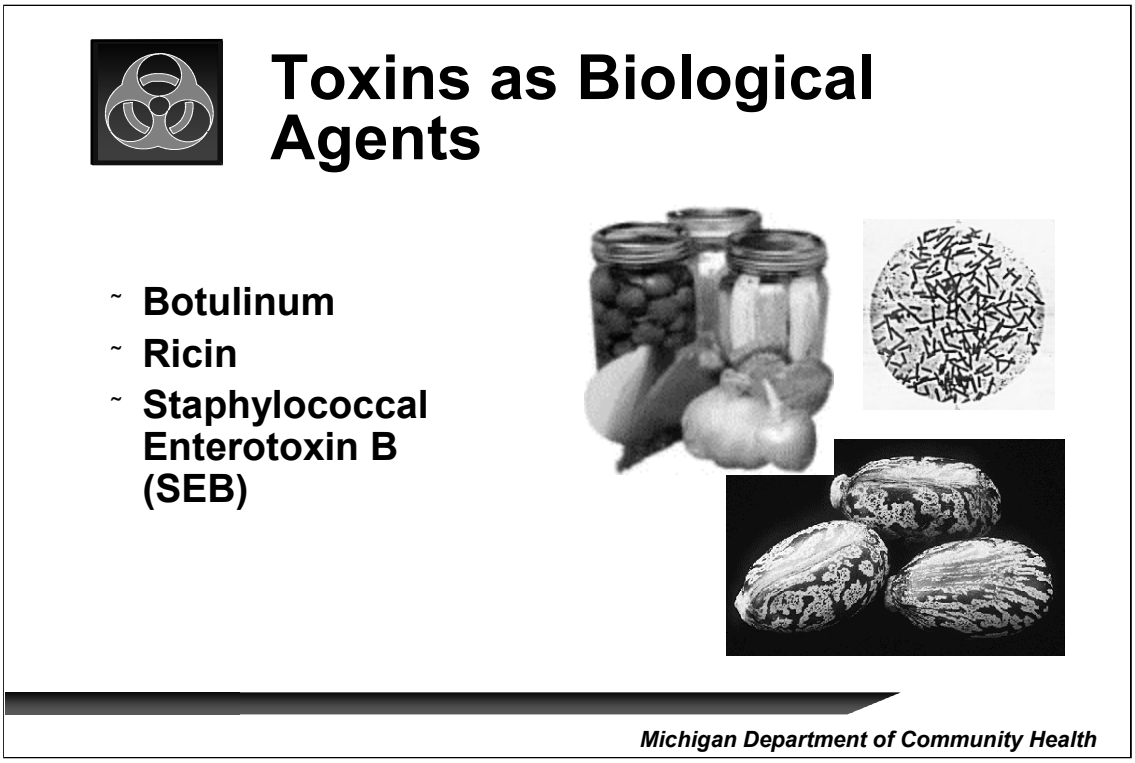
The chart above lists the specimens and information related to their collection when testing for infection with Viral Equine Encephalitis (VEE).

Specimens should be stored refrigerated and can be shipped overnight at room temperature.

Specimens collected for VEE must be submitted to the Michigan Department of Community Health Regional Laboratory System or the Michigan Department of Community Health. Contact the Bureau of Laboratories (517-335-8063) for further information on testing prior to submission.

All suspected cases of Viral Equine Encephalitis should be reported **immediately** to your local health department and the Michigan Department of Community Health at the phone numbers listed above.

For further information visit our website at www.MDCH.state.mi.us.



A large variety of lethal biological toxins exist. The agents that will be discussed in this section are those which were found to have the necessary manufactured stability and effectiveness to effect a large area coverage attack and cause mass casualties. These toxins include Botulinum Toxin A, Ricin, and the incapacitating agent Staphlococcal Enterotoxin B (SEB).
These toxins produce disease effects by different mechanisms. Botulinum Toxin acts to block nerve conduction, while Ricin is a potent cytotoxin which inhibits normal protein synthesis in mammalian cells.

Botulism: Overview

- **Caused by toxin from *Clostridium botulinum***
  - toxin types A, B, E, most commonly associated with human disease
  - most potent lethal substance known to man (lethal dose 1ng/kg)
- ***C. botulinum* spores found in soil worldwide**
- **Approximately 100 reported cases/year in the U.S.**
  - infant most common (72%)
  - food borne not common
- **<u>No</u> person-to-person transmission**

Michigan Department of Community Health

Clostridium botulinum which produces botulinum toxin is found in soil throughout the world. Botulinum toxin is most potent lethal substance known to man and there are three types of this toxin commonly associated with human disease – A,B,E.

There are low levels of botulism reported in the US (~100 cases/year). 72% of these cases are reported as infant botulism and rarely is the disease transmitted via foods. Botulism is not infectious between individuals.

Botulism: Clinical Forms

- **Foodborne**
  - toxin produced anaerobically in improperly processed or **canned, low-acid foods contaminated by spores**
- **Wound**
  - toxin produced by organisms contaminating wound
- **Infant**
  - toxin produced by organisms in intestinal tract
- **Inhalation botulism**
  - No natural occurrence, developed as BW weapon

Michigan Department of Community Health

There are three naturally occuring presentations of botulism.

1. **Foodborne Botulism** occurs when a person ingests PRE-FORMED toxin that leads to illness within a few hours to days. Only foodborne botulism is a public health emergency, because it could indicate that a food is still available to other persons (besides the patient).

3. **Wound botulism** is caused by the growth of living botulism bacteria in a wound, with ongoing secretion of toxin that causes the paralytic illness. In the United States, this syndrome is seen almost exclusively in injecting drug users.

3. **Infant botulism is a condition that** occurs in a small number of susceptible infants each year. For unknown reasons the botulism bacteria is able to grow in their intestines. Infant botulism is not a public health emergency because the infants are not consuming food with toxin; rather they are consuming *C. botulinum spores*, but for unknown reasons these few infants are susceptible to gut colonization.

Inhalational botulism does not occur naturally but may be a potential bioterrorist threat. Botulinum toxin was developed as an aerosol weapon by several countries. No human data exist on the effects inhaling botulinum toxin, but it may resemble the foodborne syndrome.

Botulism: Clinical Presentation

- **Incubation: 18 to 36 hours (dose dependent)**
- **Afebrile, alert, oriented; normal sensory exam**
  - Early nausea, vomiting, diarrhea
- **Cranial Nerve symptoms**
  - Ptosis, blurry/double vision, difficulty swallowing/talking, decreased salivation
- **Motor symptoms (progressive)**
  - Bilateral descending flaccid paralysis --> respiratory paralysis
- **Death 60% untreated; <5% treated**

Michigan Department of Community Health

Clinical onset of symptoms are dependent on dose of toxin

Early symptoms can include nausea, vomiting, diarrhea. Progressive symptoms of botulism include double vision, blurred vision, drooping eyelids, slurred speech, difficulty swallowing, dry mouth, muscle weakness which always descends the body:first shoulders, then upper arms, then lower arms, then thigh, calves, etc. Paralysis of breathing muscles can lead to respiratory failure and death unless mechanical respiration is provided. For foodborne botulism, symptoms begin from six hours up to two weeks after eating toxin-containing food; most commonly the delay is about 12-36 hours. Infants with botulism appear lethargic, feed poorly, are constipated, and have a weak cry and muscle tone.

There is a very high mortality without treatment/supportive care.

Botulism: Differential Diagnoses

- **Neuromuscular disorders**
  - Stroke syndrome
  - Myasthenia gravis
  - Guillain-Barre syndrome (Miller-Fisher variant)
  - Tick paralysis
  - Atropine poisoning
  - Paralytic shellfish/puffer fish poisoning
- **Diagnosis based on clinical history and physical exam**

Michigan Department of Community Health

Differential diagnosis includes other disorders with progressive neurologic symptoms and/or paralysis such as:

stroke syndrome

acute exacerbation of Myesthenia gravis

Guillane-Barre

Atropine poisioning

paralytic shellfish or puffer fish poisoning

Diagnosis is based on the clinical symptoms and physical exam. Detection of the toxin or organism in serum, stool, or gastric aspirates takes too long and is not always accurate.

Botulism: Treatment/Prophylaxis

- Ventilatory assistance and supportive care
- Botulinum antitoxin
  - Trivalent equine product against types A,B, and E currently available from CDC
  - Most effective if given early
- Antibiotics for infant/wound botulism
  - PCN
- Recovery may be prolonged with supportive care necessary
- Vaccine investigational, not available

Michigan Department of Community Health

Treatment of botulism involves the use of antitoxin in conjunction with supportive care. CDC maintains the national botulism anti-toxin supply. A physician diagnosing a case of botulism and wishing to treat the patient with anti-toxin must contact the CDC through their state health department. This way public health officials are alerted immediately about potential cases of botulism. Penicillin can also be used for wound or infant botulism to kill organism that is producing toxin.

**These treatments are not generally recommended for women and children. Their use in a specific clinical setting must be decided upon the basis of their risk versus the benefit to the patient.

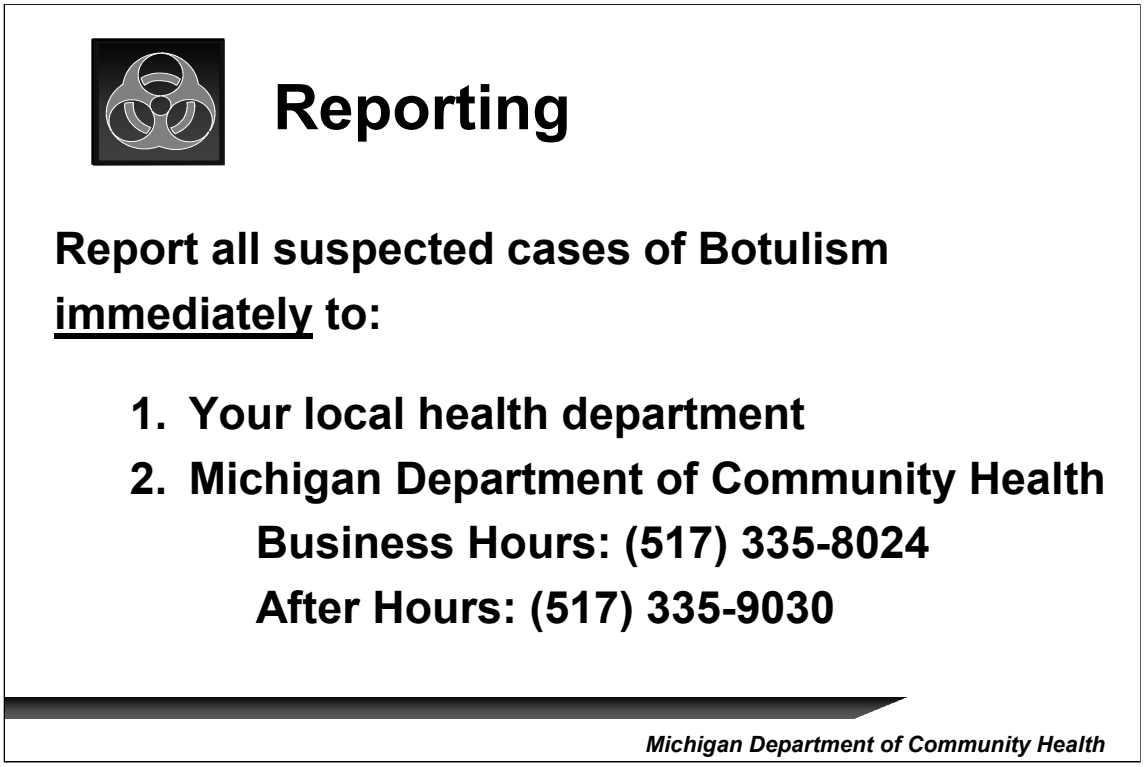
Specimen Collection: *C. boltulinum*

Specimen	Comments
	Testing must be arranged with MDCH prior to specimen transport (517/335-8063)
Serum	Collect 10 ml (3-4 ml minimum) of serum as soon as possible after the onset of symptoms and before administration of antitoxin.
Feces	15 – 25 g of stool should be collected. Store and ship at 4°C. DO NOT FREEZE. Do not use preservative.
Food sample	Requires 0.5 cup of food. Food should be left in original container if possible or placed in a sterile unbreakable container. Place containers in leak-proof plastic bags. Store and transport at 4°C. If product was originally frozen, do not thaw, ship frozen.
Wound or tissue	Place in an anaerobic collection device. Transport at room temperature.

Michigan Department of Community Health

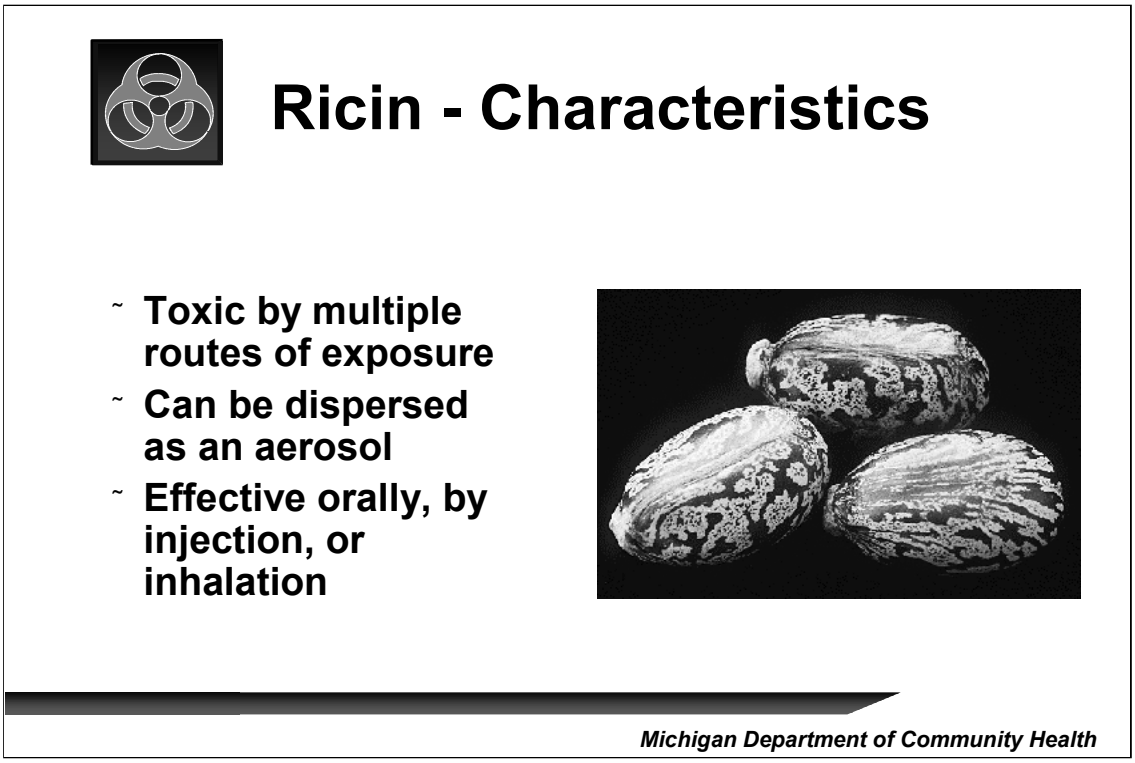
The chart above lists the specimens and information related to their collection when testing for infection with *C. botulinum*.

Specimens submitted for C. botulinum must be preauthorized by the Michigan Department of Community Health. Contact the Bureau of Laboratories (517-335-8063) for further information on testing.



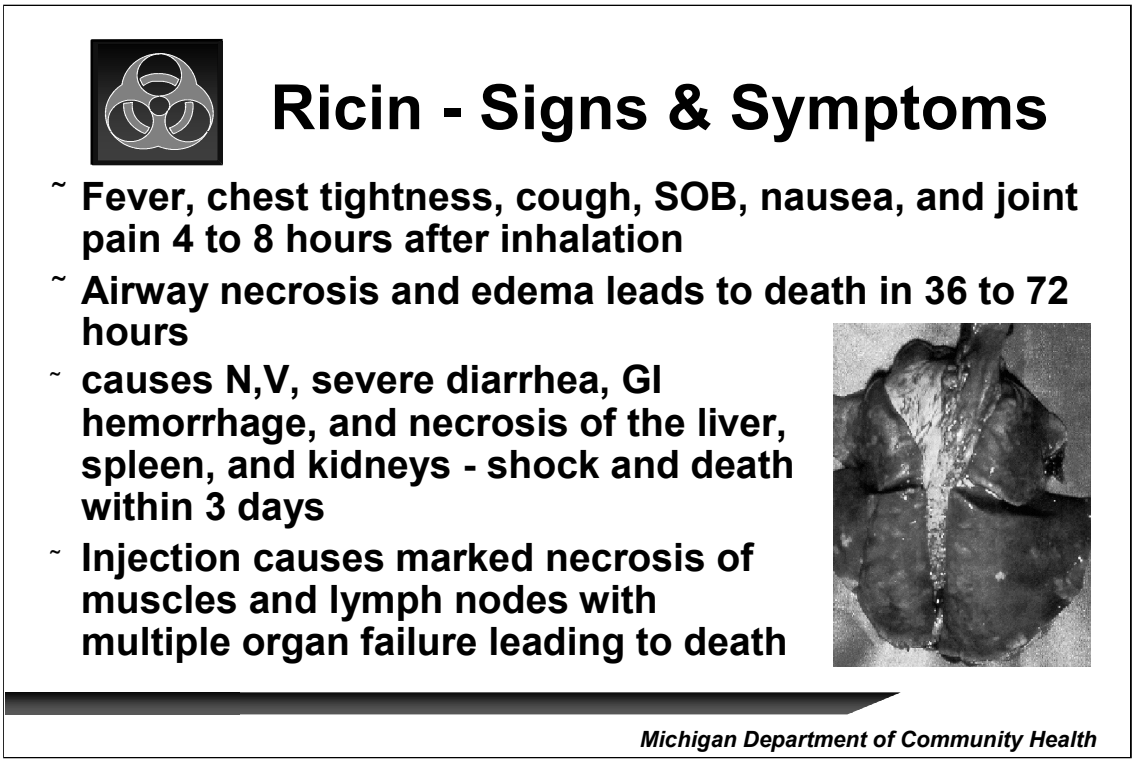
All suspected cases of Botulism should be reported **immediately** to your local health department and the Michigan Department of Community Health at the phone numbers listed above.

For further information visit our website at www.MDCH.state.mi.us.



Ricin is a lethal cytotoxin that is derived from castor beans and is a by-product of castor oil production. Over a million tons of castor beans are processed yearly into castor oil. The Ricin by-product is 200 times more toxic by weight than VX nerve agent.

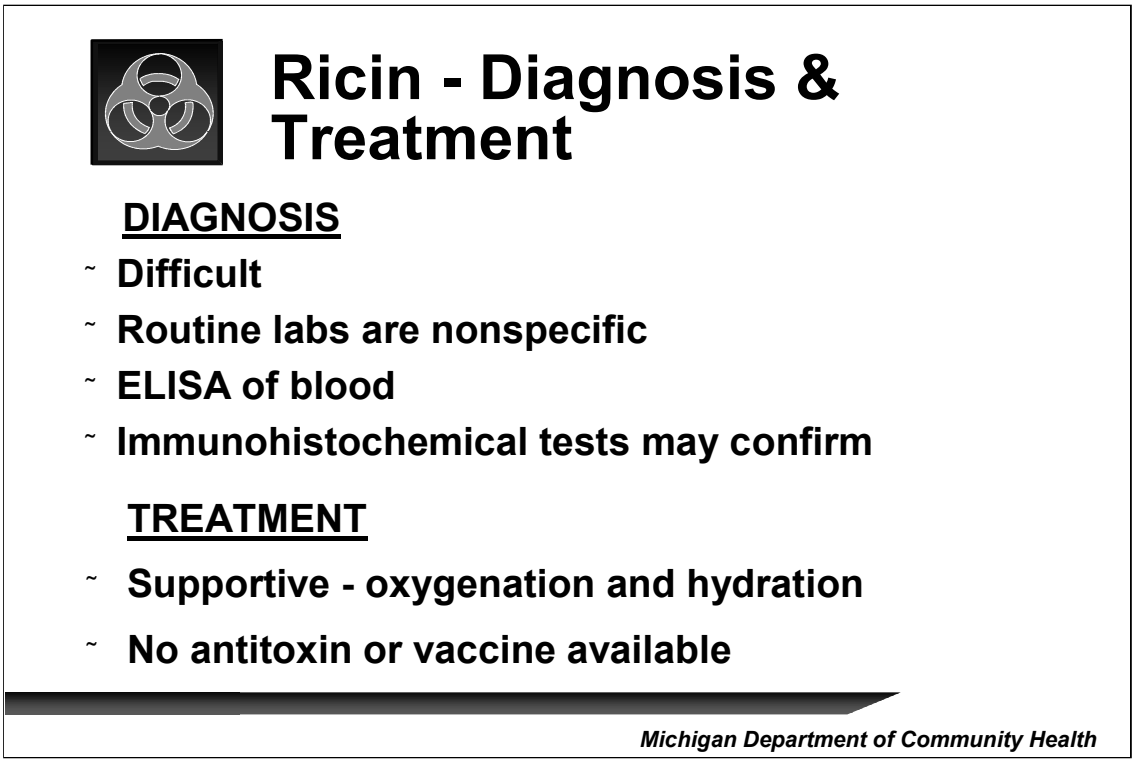
Ricin is an extremely stable compound and is toxic by multiple routes of exposure. It can be dispersed as an aerosol and is effective orally or by injection. Direct exposure to the skin is ineffective.



Within 4 to 8 hours of inhalation, victims would begin to experience fever, chest tightness, cough, shortness of breath, nausea, and joint pain. Ricin appears to cause necrosis of the lower airway epithelium and severe pulmonary edema following aerosol challenge in experimental animals. Death may occur in 36 to 72 hours. If ricin is ingested, victims often develop rapid onset of nausea, vomiting, severe diarrhea, and gastrointestinal hemorrhage with necrosis of the liver, spleen, and kidneys. Shock typically ensues with death occurring in 3 days. By injection, ricin causes marked death of muscles and lymph nodes near the site of injection along with multiple organ failure leading to death.

[Picture-RICIN – PATHOGENESIS]

Ricin exerts its toxic effect on mammalian cells by inducing a block in protein synthesis, which results in cell death. When injected, the toxin acts to destroy local tissue areas and the blood vessels in the body. This process is highly dose dependent. Severe pulmonary damage can occur when Ricin is inhaled as a small particle aerosol. The picture demonstrates a mammalian lung exposed to a bioaerosol containing ricin. The lungs are edematous with accompanying hemorrhage and necrosis and the air spaces are consolidated by a fibropurulent pneumonia. In addition, the toxin causes massive necrosis in the epithelium of the upper airway.

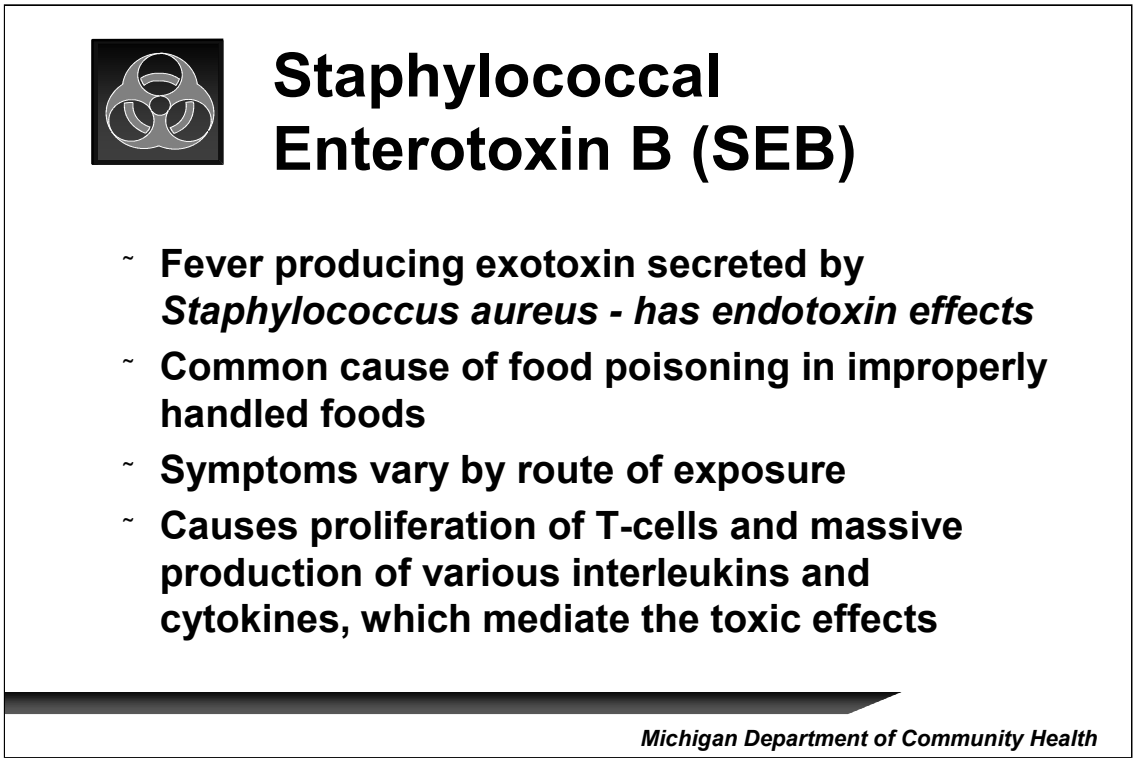


Diagnosis is often difficult since most routine laboratory findings are nonspecific. ELISA testing of blood or immunohistochemical techniques may be used to confirm ricin intoxication.

Treatment is supportive, ensuring adequate oxygenation and hydration. Gastric lavage and activated charcoal are probably indicated following accidental ingestion. No antitoxin or vaccine is currently available. If death has not occurred within 3 to 5 days, the patient usually recovers.

NOTE: Clinically, ricin inhalation will appear to be very similar to other inhaled corrosives such as phosgene.

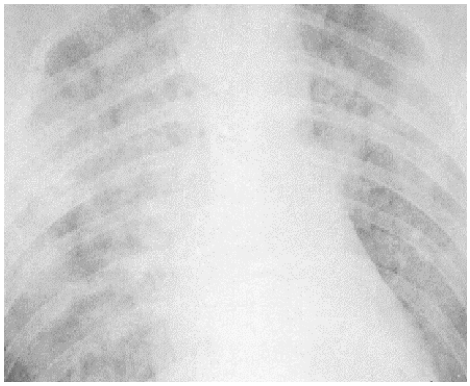
All suspected cases of Ricin should be reported **immediately** to your local health department and the Michigan Department of Community Health at the phone numbers listed above.



Staphylococcal Enterotoxin B (SEB) is a fever producing exotoxin (secreted from the organism) produced by the bacteria, *Staphylococcus aureus*. This toxin commonly causes food poisoning in improperly handled foods that have an overgrowth of the staph organism and then are ingested. SEB symptoms will vary with the route of exposure (inhaled versus ingested). Inhalation of SEB does not occur naturally and the only experience is with animal models. The toxin overstimulates certain components of the immune system, which causes a large proliferation of T-cell lymphocytes and stimulates the production and secretion of various cytokines (such as tumor necrosis factor, interferon, and interleukins). These events are thought to mediate many of the toxic effects seen with SEB and a related staphylococcal toxin mediated disease called Toxic Shock Syndrome.

SEB - Inhalation Exposure

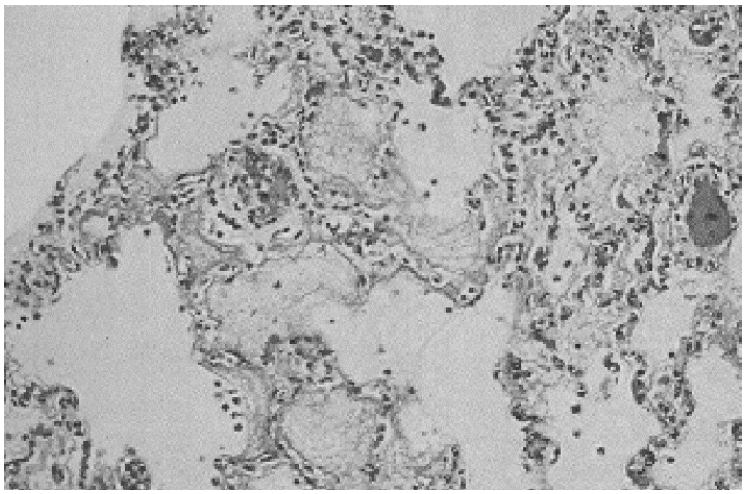
- 3 to 12 hours after inhalation
  - Sudden onset of high fever, headache, non-productive cough
- Severe SOB and chest pain
- 80% of exposed develop symptoms
- ARDS in severe exposures



Michigan Department of Community Health

The SEB toxin was developed as an incapacitating biological warfare agent, in the form of a sophisticated dry powder. The agent can be aerosolized over a large target area or introduced into a given food supply. After inhalation, the initial symptoms of aerosol intoxication would develop within 3 to 12 hours. These would include the sudden onset of fever (103^0-104^0 F), headache, chills, myalgia, and constant non-productive cough. Severe shortness of breath, chest pain, and a "toxic" pneumonia would develop in 80% of the exposed cases. High dose exposures can lead to Adult Respiratory Distress Syndrome (ARDS) and death. Nausea, vomiting, and diarrhea develop if the agent is ingested and this may also be severe. The pulmonary histology of severe cases of inhalational SEB intoxication demonstrate the intralveolar deposition of fibrin, marked perivascular interstitial edema and the focal loss of normal bronchial epithelium.

SEB – Inhalational Exposure



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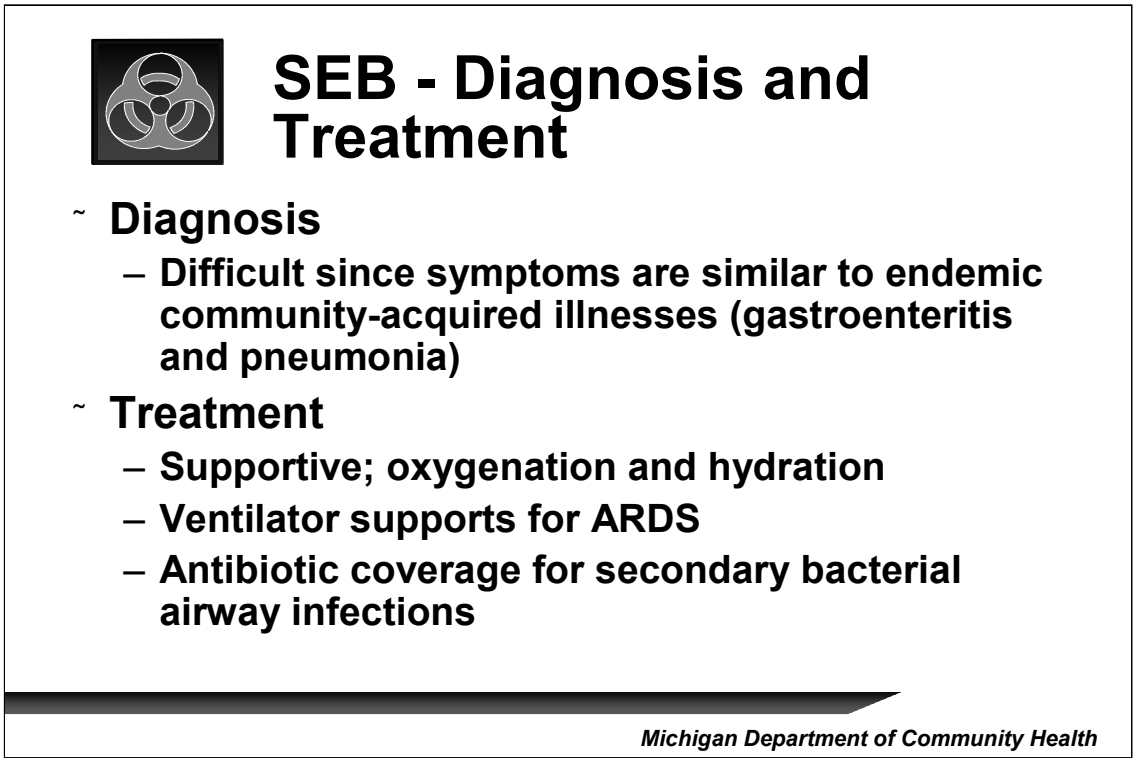
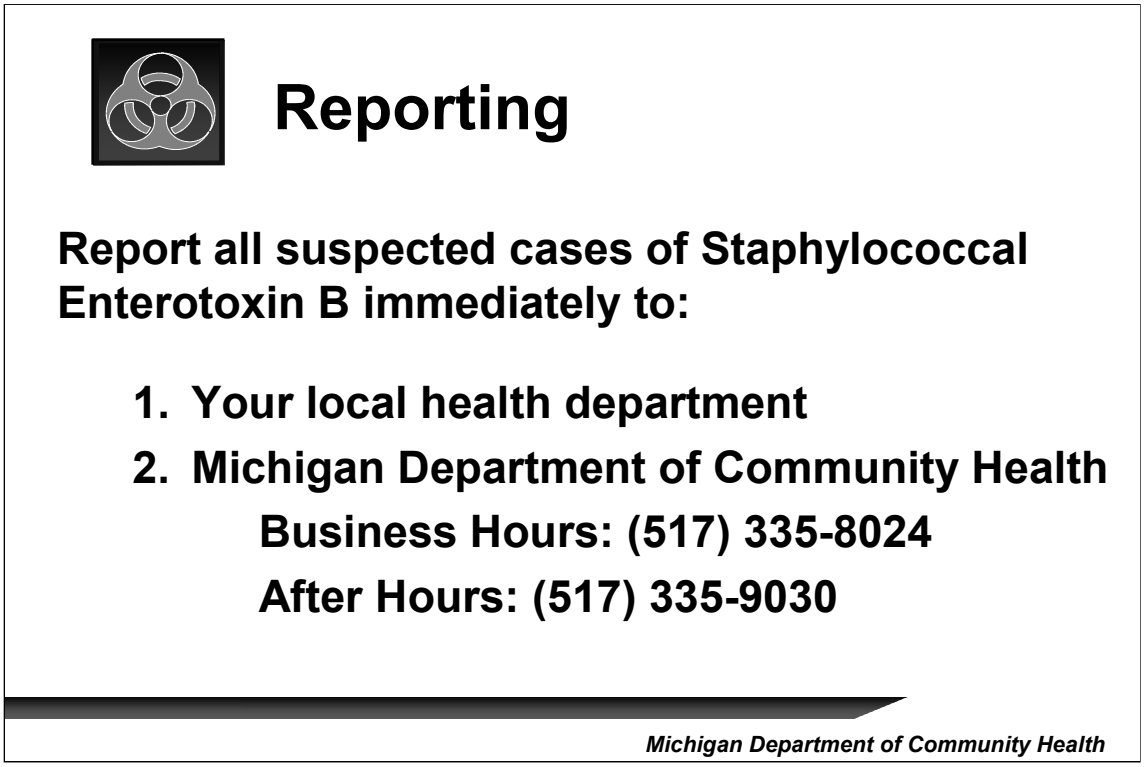
Histological section from the lung of a mammal that died of inhalational staphylococcal enterotoxin B (SEB) intoxication. There is intra-alveolar fibrin deposition and marked perivascular interstitial edema with a focal loss of normal bronchial epithelium.



A diagnosis of inhaled SEB is difficult to make because the symptoms are so markedly different from the ingested form of the illness. Early on after exposure, the symptoms of SEB will suggest an infection with typical respiratory pathogens, such as influenza, mycoplasm, and adenovirus. A diagnosis of SEB would be based on a combination of clinical and epidemiological information when large numbers of patients present with the same signs and symptoms over a 24-hour period. Patients with SEB would tend to stabilize quickly, whereas patients with pulmonary anthrax, tularemia pneumonia, or pneumonic plague will progressively worsen (and die) if untreated. The shortness of breath seen with botulism would also be associated with bulbar palsies and descending paralysis.

Treatment is supportive, with close attention to oxygen therapy and hydration. Severe cases may require ventilator support. Most victims recover after the initial phase of the illness, but this is dose related.

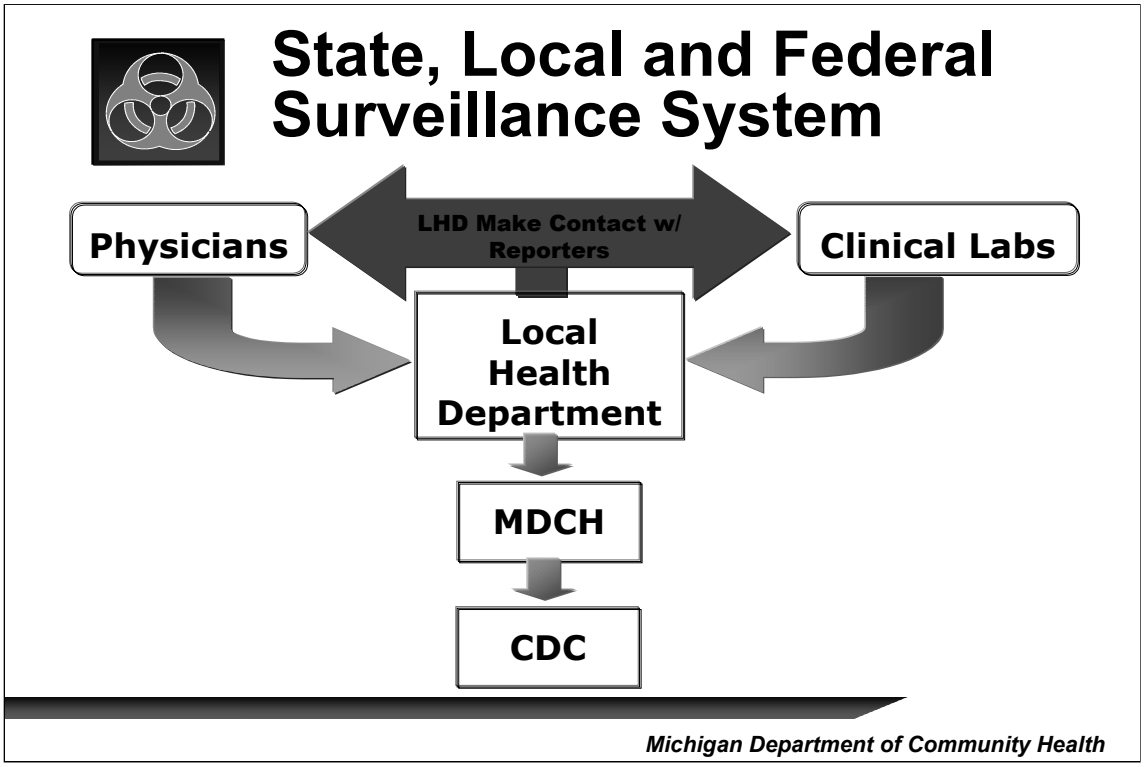


All suspected cases of Staphylococcal Enterotoxin B should be reported **immediately** to your local health department and the Michigan Department of Community Health at the phone numbers listed above.

For further information visit our website at www.MDCH.state.mi.us.

Surveillance and Reporting of Biological Agents

Michigan Department of Community Health



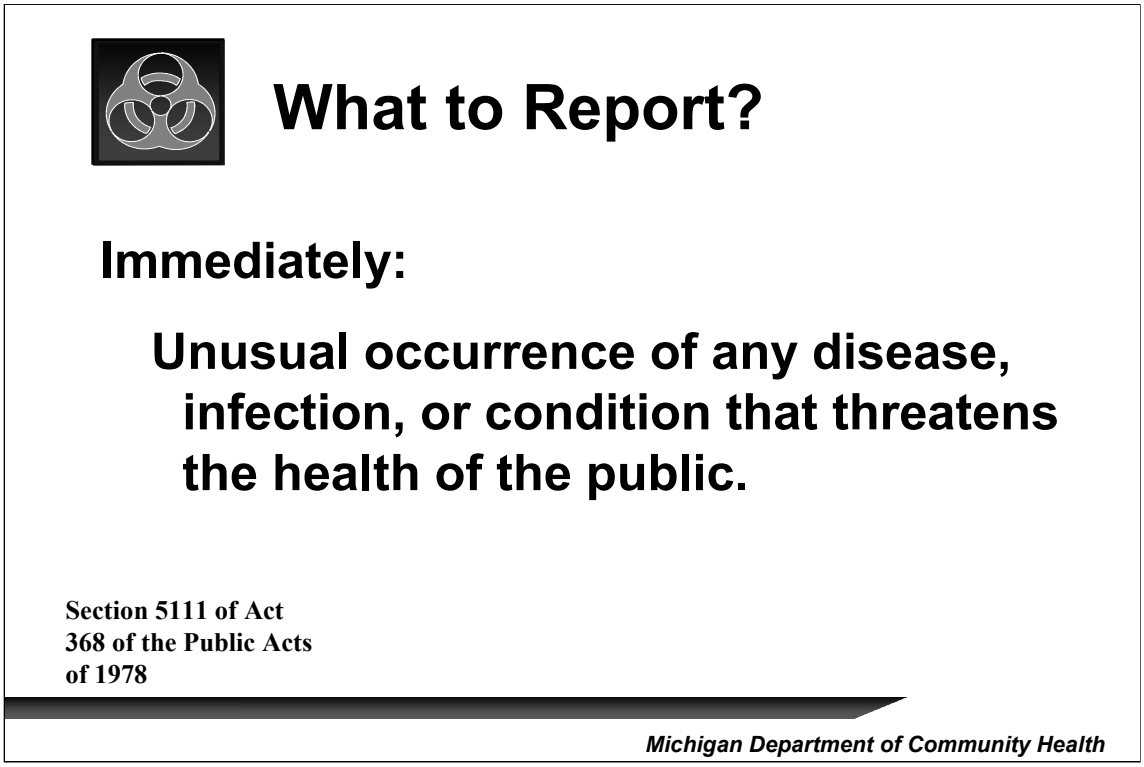
Physicians, laboratories, scientists, infection control practitioners, and other care providers play a key role in state and local health department efforts to control communicable diseases. The public health system depends upon their reports of diseases to monitor the health of the community and to provide the basis for preventive action.

Physicians and clinical laboratories are required by state law (Act. No. 368 of the Public Acts 1978, Section 5111, Michigan Communicable Disease Rules) to report serious communicable diseases and infections to local health departments. Physicians are required to report 77 different diseases and conditions. Additionally, clinical laboratories are required to report 42 infectious agents if the laboratory confirms their presence in an individual.

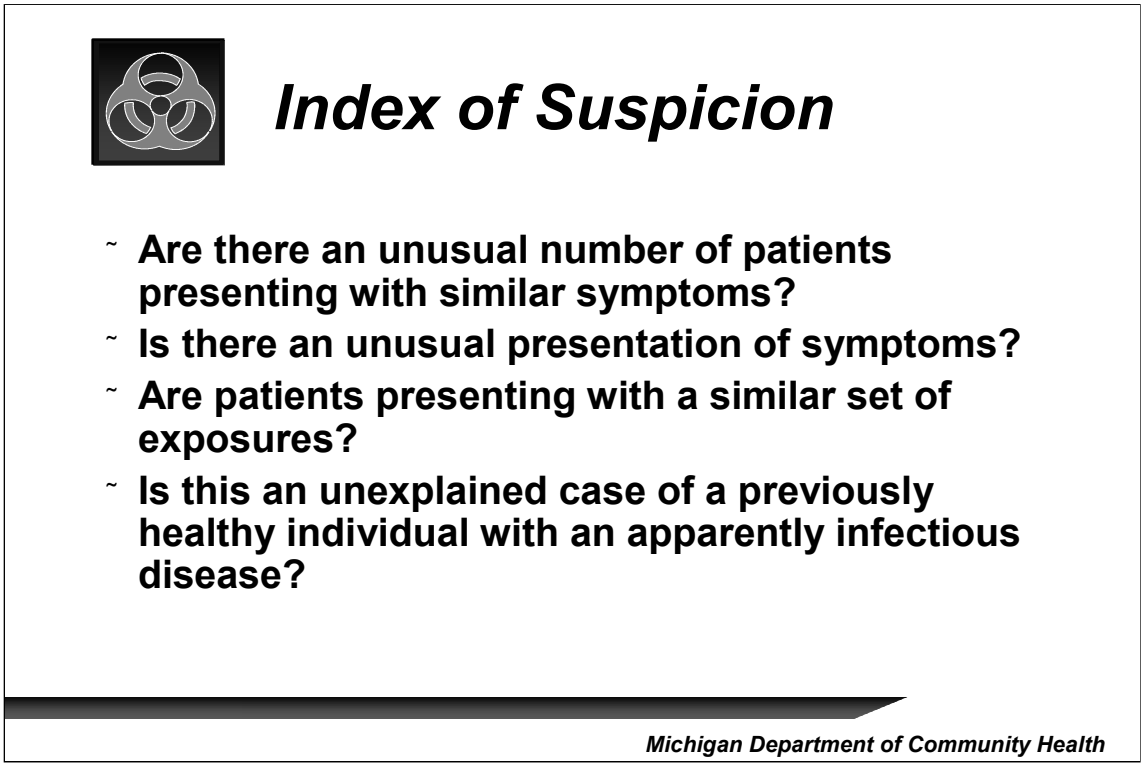
Other health care providers, including administrators, epidemiologists, infection control practitioners, dentists, nurses, pharmacists, physician's assistants, veterinarians, emergency service personnel, and any other health care professional are authorized to report these disease or conditions to local health authorities.

Providers are required to report these diseases and conditions to the local health department serving their jurisdiction or local health department serving the jurisdiction of the patient's residence. Local Health Departments in turn are required to report this information to the Michigan Department of Community Health. Information of national interest is forwarded to the Centers for Disease Control and Prevention to assist with national and international disease surveillance efforts.

This information provides the public health community with the information necessary to monitor disease trends in Michigan. It allows for early identification of outbreaks and epidemics and thus timely intervention to protect the health of the citizens of Michigan.



The Michigan Communicable Disease rules identify most of the biological agents discussed in this presentation as "serious communicable diseases" which must be reported within 24 hours. This includes any patients presenting with symptoms suspected of, or resulting from, a deliberate exposure to a biological agent. This information is required to be reported immediately to the local health department and/or the Michigan Department of Community Health



Always maintain an Index of Suspicion even if screening or confirmatory laboratory work has not been completed. What are the Zebra's?

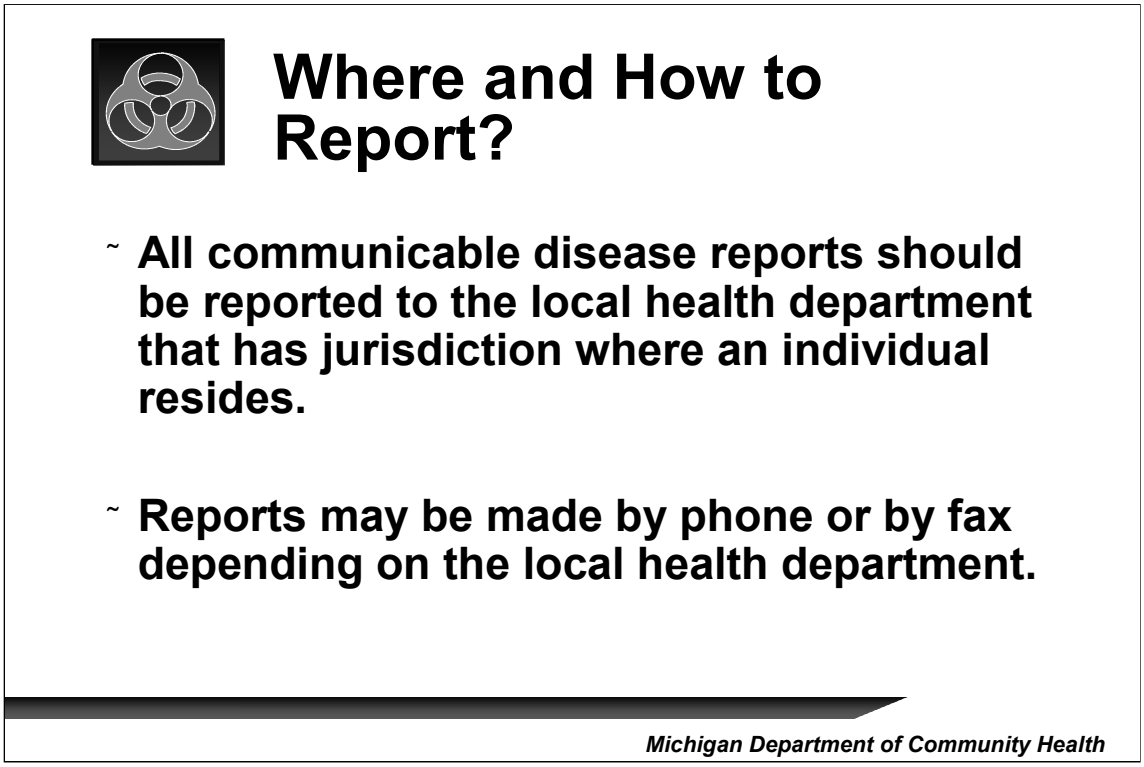
•Are there an unusual number of patients presenting with similar symptoms?

•Is there an unusual presentation of symptoms?

•Are patients presenting with a similar set of exposures?

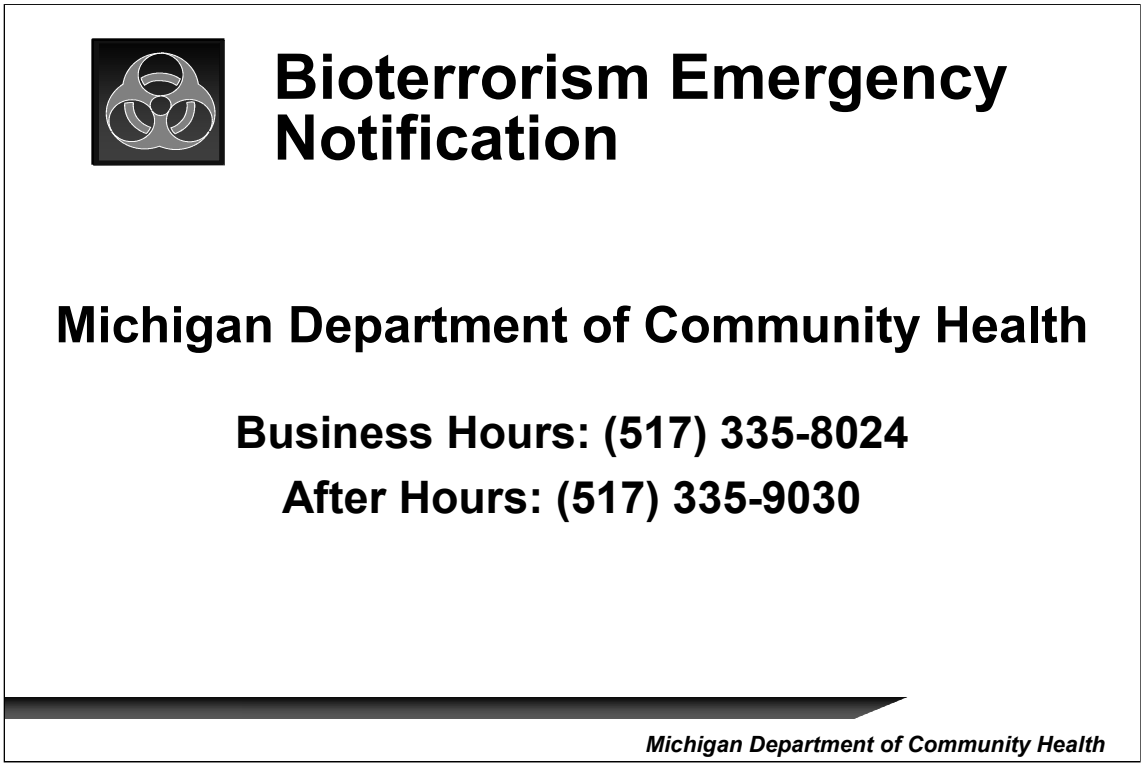
•Is this an unexplained case of a previously healthy individual with an apparently infectious disease?

Positive responses to these questions meet the standard for required reporting.



All communicable diseases required to be reported must be reported to the local health department. A list of all diseases, conditions and infectious agents that are required to be reported can be obtained from the local public health department.

Various options exist for reporting, whether by phone or fax. Contact your local health department for additional reporting options and requirements.



In the event of an actual or threatened event please notify your local health department and the Michigan Department of Community Health at the phone numbers listed above.

Acknowledgements

Michigan Department of Community Health, Bureau of Epidemiology

Michigan Department of Community Health, Bureau of Laboratories

Centers for Disease Control and Prevention

SBCCOM Domestic Preparedness Training Program

John Hopkins Center for Civilian Biodefense Studies

Michigan Terrorism Taskforce Medical Subcommittee

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Appendices

Appendix A

Directory of Michigan Local Health Departments By County

DIRECTORY OF MICHIGAN HEALTH DEPARTMENTS BY COUNTY

In general, health care providers should seek consultation regarding communicable disease prevention and control services through their local health department.

Please check your phone directory to see if there is a branch office in your community if the number listed is long distance. Write that number here: _____

COUNTY	HEALTH DEPT.	COUNTY OFFICE	AREA	PHONE	FAX	COUNTY	HEALTH DEPT.	COUNTY OFFICE	AREA	PHONE	FAX
Alcona	District 2	Harrisville	517	724-6757/5411	724-9975	Lake	District 10	Baldwin	231	745-4663	745-2501
Alger	LMAS DHD	Munising	906	387-2297	387-2224	Lapeer	Lapeer County	Lapeer	810	667-0391	667-0232
Allegan	Allegan County	Allegan	616	673-5411	673-4172	Leelanau	Benzie-Leelanau	Lk Leelanau	231	256-0200	256-0225
Alpena	District 4	Alpena	517	356-4507	354-0855	Lenawee	Lenawee County	Adrian	517	264-5203	264-0790
Antrim	NW MI Com Health	Bellaire	231	533-8670	533-8450	Livingston	Livingston County	Howell	517	546-9850	546-6995
Arenac	Cent MI DHD	Standish	517	846-6500	846-0431	Luce	LMAS DHD	Newberry	906	293-5107	293-5453
Baraga	Western UP Dist	Hancock	906	524-6142	524-6144	Mackinac	LMAS DHD	St. Ignace	906	643-1100	643-7719
Barry	Barry-Eaton DHD	Hastings	616	945-9516	945-4304	Macomb	Macomb County	Mt. Clemens	810	469-5473	493-0075
Bay	Bay County	Bay City	517	895-4001	895-4014	Manistee	District #10	Manistee	231	723-3595	723-0150
Benzie	Benzie-Leelanau DHD	Benzonia	231	882-4409	882-2204	Marquette	Marquette County	Negaunee	906	475-5765	475-9312
Berrien	Berrien County	Benton Harbor	616	926-7121	926-8129	Mason	District #10	Ludington	231	845-7381	845-0438
Branch	Branch/Hills/St Jo	Coldwater	517	279-9561	278-2923	Mecosta	District #10	Big Rapids	231	592-0130	796-7864
Calhoun	Calhoun County	Battle Creek	616	966-1236	966-1620	Menominee	Pub Hlth Delta &Men	Menominee	906	863-4451	863-7142
Cass	VanBuren-Cass DHD	Cassopolis	616	445-5280	445-5278	Midland	Midland County	Midland	517	832-6665	837-6524
Charlevoix	NW MI Community	Charlevoix	231	547-6523	547-6238	Missaukee	District #10	Lake City	231	839-7167	839-7908
Cheboygan	District 4	Cheboygan	231	627-8850	627-9466	Monroe	Monroe County	Monroe	734	240-7832	240-7906
Chippewa	Chippewa County	Sault Ste. Marie	906	635-1566	635-1701	Montcalm	Mid-Mich DHD	Stanton	517	831-5237	831-5522
Clare	Cent MI DHD	Harrison	517	539-6731	539-4449	Montmorency	District 4	Atlanta	517	785-4428	785-2217
Clinton	Mid-Mich DHD	St. Johns	517	224-2195	224-4300	Muskegon	Muskegon Co	Muskegon	231	724-4421	724-6674
Crawford	District 10	Grayling	517	348-7800	348-5346	Newaygo	District 10	Big Rapids	231	689-7300	689-7382
Delta	Pub Hlth Delta & Men	Menominee	906	786-4111	786-1962	Oakland	Oakland County	Pontiac	248	858-1286	858-0178
Dickinson	Dick-Iron Dist	Iron River	906	265-9913	265-2950	Oceana	District 10	Hart	231	873-2193	873-4248
Eaton	Barry-Eaton DHD	Charlotte	517	543-2430	543-0451	Ogemaw	District 2	West Branch	517	345-5020	345-7999
Emmet	NW MI Community	Petoskey	231	347-6014	347-2861	Ontonagon	Western UP Dist	Ontonagon	906	884-4485	884-2358
Genesee	Genesee County	Flint	810	257-1017	257-3241	Osceola	Cent MI Dist	Reed City	231	832-5532	832-1020
Gladwin	Cent MI DHD	Gladwin	517	426-9431	426-6952	Oscoda	District 2	Mio	517	826-3970	826-5386
Gogebic	Western UP Dist	Bessemer	906	667-0200	667-0020	Otsego	NW MI Dist	Gaylord	517	732-1794	732-3285
Gd Trav.	Grand Traverse Co.	Traverse City	231	922-2759	922-2719	Ottawa	Ottawa County	Holland	616	396-5266	393-5659
Gratiot	Mid-Mich DHD	Ithaca	517	875-3681	875-3747	Pres. Isle	District 4	Rogers City	517	734-4723	734-3866
Hillsdale	Branch/Hills/St Jo	Hillsdale	517	437-7395	437-0166	Roscommon	Cent MI Dist	Prudenville	517	366-9166	366-8921
Houghton	Western UP DHD	Hancock	906	482-7382	482-9410	Saginaw	Saginaw Co	Saginaw	517	758-3887	758-3859
Huron	Huron Co	Bad Axe	517	269-9721	269-4181	St. Clair	St. Clair Co	Port Huron	810	987-9396	985-2150
Ingham	Ingham Co	Lansing	517	887-4300	887-4310	St. Joseph	Branch/Hills/St Jo	Three Rivers	616	273-2161	273-2452
Ionia	Ionia Co	Ionia	616	527-5339	527-8208	Sanilac	Sanilac	Sandusky	810	648-4098	648-5276
Iosco	District 2	Tawas City	517	362-6183/84	362-7181	Schoolcraft	LMAS DHD	Manistique	906	341-4102	341-5230
Iron	Dick-Iron DHD	Stambaugh	906	265-9913	265-2950	Shiawassee	Shiawassee Co	Corunna	517	743-2318	743-2357
Isabella	Cent MI DHD	Mt. Pleasant	517	773-5921	773-4319	Tuscola	Tuscola Co	Caro	517	673-8114	673-7490
Jackson	Jackson Co	Jackson	517	788-4420	788-4373	Van Buren	VanBur-Cass DHD	Hartford	616	621-3143	621-2725
Kalamazoo	Kalamazoo Co	Kalamazoo	616	373-5267	373-5115	Washtenaw	Washtenaw Co	Ypsilanti	734	484-7200/4190	481-2498
Kalkaska	District 10	Kalkaska	231	258-8669	258-2805	Wayne (out-Wayne)	Wayne Co	Wayne	734	727-7000	727-7083
Kent	Kent Co	Grand Rapids	616	336-3425	336-2432	Detroit	Detroit City	Detroit	313	876-4138	876-0070
Keweenaw	Western UP DHD	Hancock	906	482-7382	482-9410	Wexford	District 10	Cadillac	231	775-9942	775-5372

Appendix B

Physician Disease Reporting List

Michigan Department of Community Health

PHYSICIAN - DISEASE REPORTING

All Michigan physicians and health care providers are required[1] to report patients with the following conditions to the patient's local health department. To assist health care providers in meeting their obligations to report, the Michigan Department of Community of Health has prepared the list presented below. Lab-confirmed and clinical diagnosis are reportable in the time intervals listed. Reporting allows for appropriate public health follow-up for your patients and assists us in identifying outbreaks not always evident to a sole provider.

Local Health Dept. Phone: (____) _____ Contact Name: _____
(see reverse)

IMMEDIATELY

Any unusual occurrence, outbreak, or epidemic of any disease, condition, and/or nosocomial infection.

WITHIN 24 HOURS

AIDS	Granuloma inguinale	Plague
Anthrax	*H. influenzae* (meningitis or epiglottitis)	Poliomyelitis
Botulism	Hepatitis B in a pregnant woman	Rabies (human)
Chancroid	Lymphogranuloma venereum	Syphilis
Cholera	Measles	Tuberculosis
Diphtheria	Meningococcal disease (meningitis or meningococcemia)	Viral hemorrhagic fevers
Gonorrhea	Pertussis	Yellow fever

WITHIN THREE WORKING DAYS

Amebiasis	Hepatitis	Rubella
Blastomycosis	Histoplasmosis	Salmonellosis
Brucellosis	Kawasaki disease	Shigellosis
Campylobacter enteritis	Legionellosis	Staphylococcal disease, (first 28 days post-partum mother or child)
Chlamydia (genital)	Leprosy	Streptococcal, invasive Group A (normally sterile sites)
Coccidioidomycosis	Leptospirosis	Tetanus
Cryptococcosis	Listeriosis	Toxic shock syndrome
Cryptosporidiosis	Lyme disease	Trachoma
Cyclosporiasis	Malaria	Trichinosis
Dengue fever	Meningitis (bacterial & viral)	Tularemia
E. coli disease (**only** shiga toxin producers)	Mumps	Typhoid fever
Ehrlichiosis	Psittacosis	Typhus
Encephalitis, viral	Q fever	*Yersinia* enteritis
Giardiasis	Reye's syndrome	
Guillain-Barrer syndrome	Rheumatic fever	
Hantavirus pulmonary syndrome	Rocky Mountain spotted fever	
Hemolytic-uremic syndrome	Rubella (congenital syndrome)	

WITHIN ONE WEEK

HIV Infection	Chicken pox (aggregate numbers)	Influenza (aggregate numbers)

HOW TO REPORT
Call, mail or fax your local health department
Provide patient demographics, diagnosis and onset date

1 Communicable Disease Rules
R 325.171 et al

11/99

Appendix C

Laboratory Disease Reporting List

MICHIGAN DEPARTMENT OF COMMUNITY HEALTH

LABORATORY - DISEASE REPORTING

All Michigan laboratories are required[1] to report patients with the following conditions to the patient's local health department. To assist health care providers in meeting their obligations to report, the Michigan Department of Community of Health has prepared the list presented below. Reporting allows for appropriate public health follow-up for your patients and assists us in identifying outbreaks not always evident to a sole provider.

Local Health Dept. Phone: (_____) (see reverse) Contact Name: _____

IMMEDIATELY

Any unusual occurrence, outbreak, or epidemic of any disease, condition, and/or nosocomial infection.

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WITHIN 24 HOURS

Bacillus anthracis	Hemorrhagic fever viruses	Rabies virus
Bordetella pertussis	Hepatitis B surface antigen	*Treponema pallidum*
Calymmatobacterium granulomatis	Measles (Rubeola) virus	*Vibrio cholerae,* serovar 01
Clostridium botulinum	*Mycobacterium tuberculosis*	Yellow fever virus
Corynebacterium diphtheriae	*Neisseria gonorrhoeae*	*Yersinia pestis*
Haemophilus ducreyi	*Neisseria meningitidis* (sterile sites)	
Haemophilus influenzae type b (sterile sites)	Poliovirus	

WITHIN THREE WORKING DAYS

Arboviruses	*Francisella tularensis*	*Plasmodium* species
Borrelia burgdorferi	*Giardia lamblia*	Rubella virus
Brucella species	Hantavirus	*Salmonella* species
Campylobacter jejuni	Hepatitis A (anti-HAV IgM)	Shiga toxin producing *E. coli* disease
Chlamydia species	Influenza virus	*Shigella* species
Cryptosporidium species	*Legionella* species	*Trichinella spiralis*
Cyclospora species	*Listeria monocytogenes*	*Yersinia enterocolitica*
Entamoeba histolytica	Mumps virus	

1 Communicable Disease Rules R 325.171 et al

HOW TO REPORT
Call, mail or fax your local health department
Provide patient demographics, diagnosis and onset date

10/99

Appendix D

Treatment, Prophylaxis and Vaccination Guidelines for Critical Biologic Agents

Treatment, Prophylaxis and Vaccination Guidelines for Critical Biologic Agents

DISEASE	Treatment	Prophylaxis	Vaccine
Inhalation Anthrax	1) *Ciprofloxicin 400 mg IV q 8-12 h 2) *Doxycycline 100 mg IV, then 100 mg q 8-12 h 3) Penicillin G 4 million units IV q 4 4) Other: Erythromycin, chloramphenicol	1)*Ciprofloxicin 500 mg PO bid X 60 days w/o vaccine PO bid X 30 days w/ vaccine 2)*Doxycyline 100 mg PO bid x 60 days w/o vaccine bid x 30 days w/ vaccine	Attenuated strain of *B. anthracis*-SC dose given at 0,2, 4 wks and 6, 12, 18 mos -2 year protection -very safe
Smallpox	?Cidofovir (efficacy not proven-not recommended currently secondary to renal toxicity)	1)Vaccinia Immune Globulin 0.6 mL/kg IM (within 3 d of exposure) 2)Vaccinia vaccine if given within 7 d of exposure	Vaccinia virus intradermal -1 dose -Disseminated vaccinia infxn in 3/10,000
Plague	1) *Streptomycin 30 mg/kg/d IM in 2 divided doses for 10 d (or gentamicin) 2) *Doxycycline 200 mg IV then 100 mg IV bid x 10-14 d 3) Chloramphenicol 1 gm IV qid x 10-14 d (tx of choice for plague meningitis)	1)*Doxycycline 100 mg PO bid x 7 d 2)*Ciprofloxicin 500 mg PO bid x 7 d 3)*Tetracycline 500 mg PO qid x 7 d 4)Other: Bactrim	Vaccine no longer available (Killed whole cell vaccine was discontinued in 1999)
Tularemia	1) *Streptomycin 30 mg/kg IM qd x 10-14 d 2) Gentamicin 3-5 mg/kg/d IV x 10-14 d	1)*Doxycycline 100 mg PO bid x 14 d 2)*Tetracycline 500 mg PO qid x 14 d	Live, attenuated vaccine (IND) -given by scarification -effective vs aerosolized tularemia
Botulism	DOD heptavalent equine despeciated antitoxin for serotypes A-G (IND): 1 vial (10 mL) IV	None	Toxoid vaccine (IND) -SC injection -0,2, 12 weeks, 1 yr booster
Viral Hemorrhagic Fever	• Ribavirin (CCHF/arenaviruses) 30 mg/kg IV initial dose then 15 mg/kg IV q 6 h x 4 d then 7.5 mg/kg IV q 8 h x 6 d • Passive antiboby for AHF, BHF, Lassa fever, and CCHF	None	Yellow fever vaccine Rift Valley Fever vaccine (investigational)

IND=investigational new drug, CCHF=Congo-Crimean hemorrhagic fever, AHF=Argientine hemorrhagic fever, BHF=Bolivian hemorrhagic fever, SC=subcutaneous, tx=treatment

*These treatments are not generally recommended for women and children. Their use in a specific clinical setting must be decided upon the basis of their risk versus the benefit to the patient.